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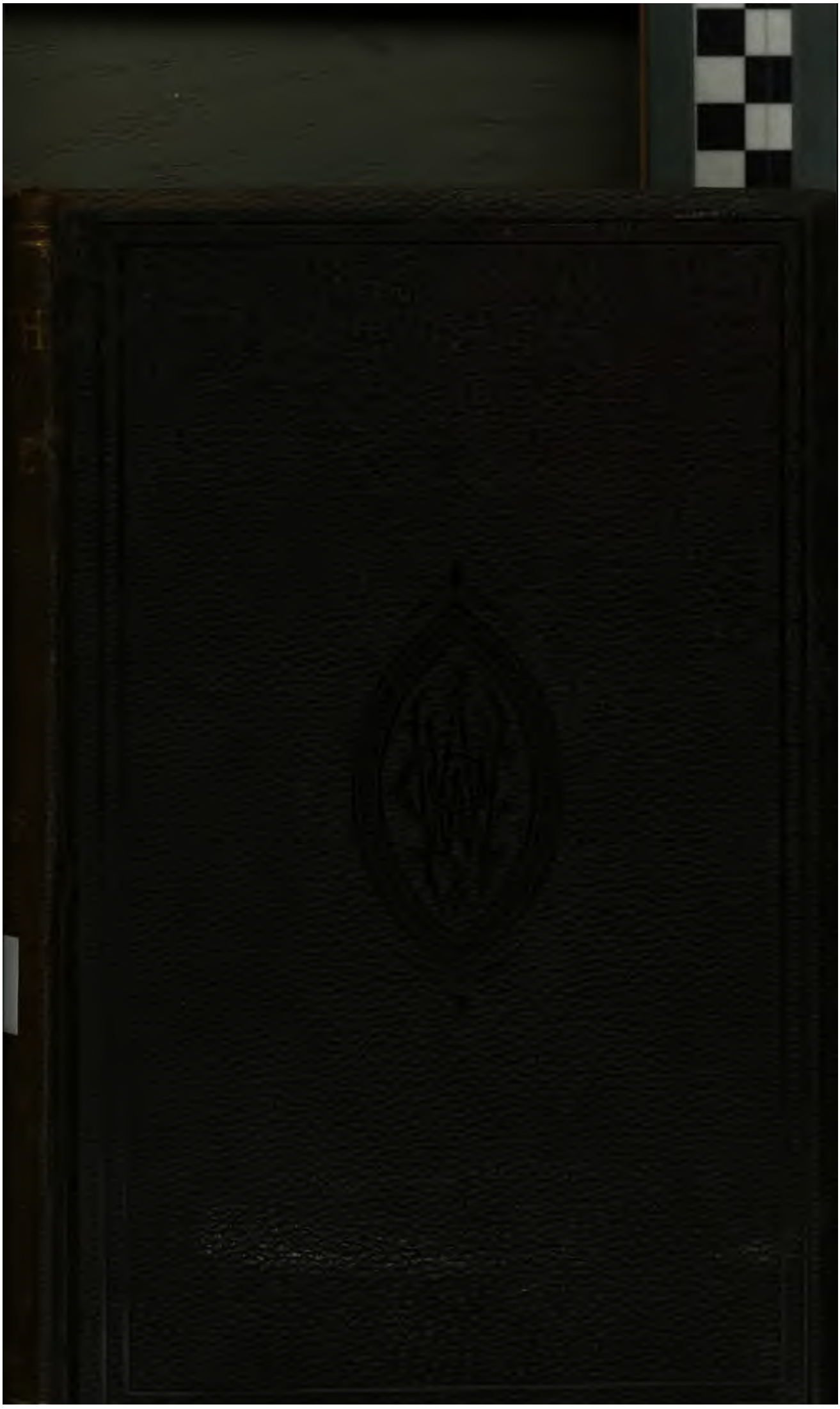

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AN INTERNATIONAL ENCYCLOPEDIA

OF

MODERN MEDICAL SCIENCE

BY

LEADING AUTHORITIES OF EUROPE AND AMERICA

EDITED BY

THOMAS L. STEDMAN, M.D.
NEW YORK CITY

IN TWENTY VOLUMES

VOLUME XV

INFECTIOUS DISEASES

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INFLUENZA.

BY

DITMAR FINKLER,

BONN.

INFLUENZA.

C. E. Reed M. D. 1898

INFLUENZA is an infectious disease which in the highest degree appeals to our interest in many directions. It at times extends pandemically, with a velocity and wide spread such as we see in no other disease at present known. Numerous phenomena of its epidemiological behavior border on the miraculous, and fill us with wonder and astonishment. On the other hand, influenza in single cases produces so manifold and often such remarkable morbid pictures, that the study of the disease, though demanding great labor, brings a rich reward eventually. In the closing years of this century influenza has given us occasion to test all the modern attainments of medical science. Physicians have labored whole-souled in the attack against this pestiferous disease and they have also worked with such ardor in the solution of the riddle which confronted them, and they have endeavored to fathom it with such an ideal working together in all directions, that it may be truly said that influenza has become the teacher in many branches of medicine, and it has demonstrated to the whole world such thoroughness of methods on the part of physicians and investigators that our profession has a right to feel proud of its members.

Epidemiology.

With the discovery of the microorganism of influenza by R. Pfeiffer in the year 1892, a milestone was reached in the history of this disease. The obscurity which shrouded the epidemics of influenza of former centuries as regards the etiology and the epidemic character of the disease, will, thanks to the researches of this savant, be lifted from future epidemics.

In former times the occurrence of epidemics was referred to coincident natural phenomena, as the appearance of comets, volcanic eruptions, earthquakes, etc., and even Webster[1] attempted to prove this association in his work on the history of epidemic diseases.

As we now approach the difficult problem of portraying the history of influenza, it seems proper in enumerating the epidemics to consider two points, namely (1) whether all the epidemics grouped

under this head in literature have been true epidemics of influenza, and (2) whether complications were prominent in these epidemics. Naturally we can find reliable data bearing upon this second point only in the accounts of influenza epidemics of the later centuries.

The first records, referring to pestilential diseases, which were regarded by historians, such as Haeser[67] and others, as descriptive of influenza, are met with in Livy,[24] and refer to a pestilence in the year 412 B.C.

An epidemic, which was not very exactly described, need not have been influenza simply because few persons died. Livy says: Pestilentia coorte minacior tamen quam perniciosa . . . perpaucis funeribus. Most[68] speaks of an influenza which is thought to have been described by Hippocrates, but Schweich mentions, as arguing against this assumption, that Hippocrates speaks of a day-blindness in this epidemic, but does not speak of important symptoms of influenza, as the involvement of the abdomen and the presence of sweats, which, had they been present, would certainly not have escaped so sharp an observer as Hippocrates. Historians, as for example Leupold[8] and Thomas Glass (see Thompson's "Annals"[1]), look upon the report of Diodorus, on a pestilence occurring 395 B.C., as having been one of influenza. The epidemic broke out in the Greek army at the siege of Syracuse, and killed off the soldiers murderously. This fact is, however, a sufficient argument against the supposition that the disease was influenza. With as little reason can an epidemic mentioned by Pasquier, which began, according to Procopus, in the reign of the Emperor Justinian in the city of Peleus in Egypt and spread over the whole earth (par tout l'univers), be looked upon as having been influenza. Pasquier says: "Le patient était affligé d'une toux extrême qui le tenait depuis le matin jusqu'au soir." The mortality was enormous; in Constantinople five thousand to six thousand citizens died from this disease in one day. A pestilence claiming so many victims has no relation to influenza.

Leupold, however, says: "By what right do we regard as true influenza only the simple and slight forms of influenza, such as we meet with commonly in modern times, when even recent epidemics have occurred in many different forms, and in part displayed a quite malignant character? Or, what other disease than influenza, although not especially mild, could it have been which occurred, for example, in the year 591 or 592 B.C., which often, when hardly ushered in by headache and coma, rapidly ended in death?"

Because of the very short and uncertain records which, as a rule, have come down to us from this olden time, it is impossible to decide whether epidemics of true influenza or of other pestilential diseases

were indicated, unless we base our judgment upon the mortality record of the various epidemics.

In like manner the following "reports found in the chronicles," as Biermer calls them, are not convincing. These were a cough which spread like the plague in 827; the so-called Italian fever which ravaged Germany and Italy in 876, accompanied by pain in the eyes and cough; the cough and fever which spread throughout Germany in 888; also the epidemics observed in Germany and France in 927, and in England in 996–997.

According to August Hirsch, the first influenza epidemic occurred in 1173, and he places it in his work[8] as the first out of eighty.

The views are, however, divided as to the occurrence of the first epidemic, as may be seen from the following table:

Year of the first influenza epidemic.	Authors.
1173	Hirsch.
1293	Zeviani.
1323	Gluge.
1387	Schweich.
	Biermer.
	Ripperger.
1510	Saillant.
	Thompson.
	Zuelzer.
	Leichtenstern.

Epidemic of 1173.

Hirsch mentions the month of December as the time of the epidemic of the year 1173, and the countries in which it prevailed as Italy, Germany, and England. His sources are, for England, Radulphus de Diceto who writes as follows: "Sub hisdem diebus universus orbis infectus ex aeris nebulosa corruptione, stomacho catarrhum causante generalem tussim, ad singulorum perniciem, ad mortem etiam plurimorum inmissam vehementer expavite." In Europe cough also was a prominent symptom in this epidemic. Thus Godefridus speaks of a "tussis intolerabilis et inaudita"; the chronicle of Saxony has it "concepta est in hominibus tussis gravissima," and another chronicle speaks of a "tussis magna."

Leichtenstern says: "A. Hirsch believes that he has found in the sparse records of the year 1173, founded upon Italian and French sources, the first positive mention of an influenza epidemic." Ripperger[18] cannot bring himself to recognize the occurrence of an influenza epidemic in 1173. As a matter of fact, the records are too

meagre and not explicit enough to prove the existence of an influenza epidemic in the year 1173, but the possibility of its existence cannot be absolutely denied.

Epidemics of 1239 and 1311.

Zeviani[8] mentions as the first epidemics those of 1239 and 1311. A positive description is not given; it is said only that a great number of people had died in the pestilential disease which in 1311 was reported to have ravaged the whole of France. On account of the very meagre description, other influenza historians, as also Hirsch, have not made any mention of these years.

Epidemics of 1323 and 1327.

Hirsch mentions as the second influenza epidemic that of the year 1323, which is the one with which Gluge begins his history of the disease. As a voucher both these authors as well as Zeviani quote Piero Buoninsegni, who writes: "In questo anno e d'Agosto fu un vento pestilenzia le per lo quale amalò di freddo e di febbre per alcuni dì quasi tutte le persone in Firenze e questo medesimo fu quasi per tutta Italia." Gluge[16] says, referring to this: "The description of the disease, its spread to persons and cities, seem to me sufficient ground to accept it as influenza." Most believes it to have been, from the symptomatic description of the Italian physician Targioni Torzetti, 1323, rather a typhoid-fever epidemic, complicated by chest affections, than a catarrhal epidemic.

For the epidemic of 1327 (according to Hirsch, 1328), Zeviani and Gluge also quote Buoninsegni, who writes: "In detto anno e mese (March) fu quasi per tutto Italia corruzione di febbre per freddo; ma pochi ne morirono." Biermer[17] regards the epidemics of 1323 and 1327 as being doubtful; Ripperger thinks they may possibly have been influenza.

For the year 1358 I find the mention of an epidemic influenza from the sources in Zeviani only. He refers back to Buoninsegni, who has the following to say about the year 1358: "Essendo stato dal principio del verno passato un tempo serenissimo comminciò . . . influenza di freddo che quasi ogni persona della città, e distretto, e d'intorno infreddorono, e molti ne morirono." We meet here with the name of "influenza," which in itself is of course no proof. Biermer says of this epidemic: "The epidemic spreading in 1357-58 over Savoy, Germany, France, Catalonia, we hold even less to have been influenza than that of 1323 and 1327." Gluge was not able to dis-

cover the passage above cited in Buoninsegni, to which Zeviani refers for the epidemic of 1358, although it is there in fact. We are ready to admit, with Gluge, that the description of Buoninsegni, of the year 1357, cited by Gluge: "Fu in detto mese grande influenza di lunghe e mortali infermità in Firenze e nel contado e morirono molti," etc., does not apply to influenza. At that time a strange law, so writes Buoninsegni, was enacted in Florence, according to which no physician was allowed to visit a patient more than twice, under penalty of a fine of 500 lire.

We have seen that the views of historians differ greatly as regards the epidemics of the years of 1173, 1239, 1311, 1323, 1327, and 1358, for the reason that the notes which are accessible to us as to their history, do not allow of a definite judgment.

Epidemic of 1387.

Zeviani, Schweich, Gluge, Hirsch, and Ripperger mention this epidemic, and Ripperger begins the history of influenza with it. The disease appeared in Italy in January and February of this year.

Buoninsegni[1] writes: "Del mese di Gennaio comminciò in Firenze una influenza, che quasi ogni persona malava di freddo e con febbre, e durò insino à mezzo febbraio e morironne molti d'ogni età, ma piu de' vecchi."

Besides Buoninsegni, Alexander Benedictus[2] also mentions that the epidemic visited Italy (omnem Italiæ oram), and Zeviani (p. 478) reports that Marchese observed it in the city of Forli, in the Romagna, when not a person escaped, although only a few died (se ben pochi ne morirono). It is uncertain whether Benedictus means this year; Zeviani (p. 479) for example quotes this passage of the epidemic of 1482: "Ætate nostra hujusmodi destillationes graves periculosæque cum acuta febri omnem Italiæ oram infestaverunt ex quodam cœlesti influxu; ita ut plurimi caderunt.

Valescus de Taranta,[3] who received his license to practise medicine in this year, observed the epidemic in Montpellier, France, and concerning it wrote: "Fuit catarrhus quasi generalis ita quod vix decima pars gentium præter infantes evasit catarrhum cum febre, et fere omnes decrepiti moriebantur propter dictam causam."

Jacob, of Königshofen, writes in the Strassburg Chronicle: "There came a general pestilence in the whole country, with *cough* and *influenza*, so that hardly one among ten remained healthy." He reports, in accord with the just mentioned Valescus, that old and debilitated persons were frequently the victims. The same is said by Buoninsegni (see above).

According to Gassar the disease, which was called by him "mira quædam epidemia," greatly ravaged southern Germany (Germania superior), especially Augsburg. The patients suffered four or at the most five days with the most disagreeable catarrhal symptoms (molestissimis destillationibus), and delirium occurred; the patients, however, recovered, and only very few were removed by death.

The fact, frequently mentioned, that hardly any one was spared by the disease, and yet it became dangerous only to a few persons, and these old ones, is greatly in favor of influenza. It is of course natural that not all the characteristic morbid symptoms are mentioned in the fragmentary records which have reached us, and it is not denied that the epidemic may have existed in other countries besides Italy, France, and Germany; we do not, however, find any further specification in literature (not even by Hirsch). Gluge says (p. 48): "However meagre the data of this epidemic may be, they sufficiently characterize influenza."

Epidemic of 1403.

This is mentioned by Gluge and Ripperger. The source is Pasquier,[9] who is the only authority for both. Pasquier says: "En Registres de Parlement on trouve que le vingt-sixième jour d'avril 1403 y eut une maladie de teste et de toux, qui courut universellement si grande, que ce jour-là le Greffier ne pût rien enrégistrer et fut-on contraint d'abandonner le plaidoyé."

Ripperger declares this report of Pasquier, "short as it is, to be extremely characteristic of influenza." Pasquier believes this epidemic to have been of the same disease as that occurring during his own life, in the year 1557. Hirsch does not mention this epidemic, nor do the older historians, as Zeviani, Most, and Schweich.

Epidemic of 1404.

Hirsch and also Ripperger mention an epidemic which, according to Baliolanus, visited the Netherlands (Flanders) and according to Hirsch (Mansfelder Chronicle) also invaded Germany (Saxony and Thuringia). Baliolanus (vulgo Jacob Meyer, according to Ripperger) writes: "Eoque frigore humanis corporibus concepto . . . tussis maxima atque raucitas orta unde nullus pene ordo, ætas et sexus liber evasit." In Flanders this epidemic reigned principio Aprilis. Cough and hoarseness are mentioned as symptoms; hardly any one escaped. I have been unable to obtain the Mansfeld Chronicle under the short title which is given to it by Hirsch.

In Baliolanus's report we have also the first mention of an epizootic present at the same time, animals being attacked by the same disease (eodem malo): "Vaccæ miserabili cum mugiti moriebantur." (In Hirsch this coincidence is mentioned first in the epidemic of 1693, on the authority of Molineux.)

Epidemic of 1411 (le Tac).

For the epidemic of 1411, we can again rely only on Pasquier,[9] a part of whose description is as follows: "En 1411 y eut une autre sorte de maladie, dont une infinité de personnes furent touchez, par laquelle l'on perdoit le boire, le manger et le dormir . . . toujours trembloit et avec se estoit si las et rompu que l'on ne l'osoit toucher en quelques parts." A violent cough disturbed the patient night and day, appetite was lost, and a violent fever (?) made its appearance after meals. The duration of the illness was three weeks; it was not, however, dangerous: "Sans qu'aucune personne en mourut." In women abortions occasionally occurred from the violence of the cough. During convalescence hemorrhages appeared from the nose, the mouth, and the rectum. The physicians had no explanation of the cause of the disease, which was called *le tac*, and it was simply referred to a "contagion générale de l'air." Pasquier does not say a word as to the extent of the epidemic; his description applies only to the disease as it occurred in Paris.

Epidemic of 1414.

The disease prevailed in Italy as well as in Paris, and according to Hirsch (p. 6) in the cities of Bologna, Forli (also mentioned by Zeviani), Venice, and Florence.

Sauval[10] says of the epidemic in Paris: "Vers le mois de mars on vit naître à Paris un autre mal appelé le tac, autrement le horion, mais qui ne dura que trois semaines."

Lobineau (quoted by Ripperger) also mentions the names *le tac* and *le horion*, in addition to which the designation *coqueluche* was employed. He describes the disease, which was nearly general during the months of February and March, in the following manner: "C'était une espèce de rhume, qui causa un tel enrouement que le chastelet furent obligez d'interrompre leurs séances; on dormoit peu et l'on souffroit de grandes douleurs à la teste, aux reins et par tout le reste du corps; mais le mal ne fut mortel que pour les vieilles gens de toute condition."

Mezeray[11] also mentions this epidemic, which he says occurred under the name of coqueluche during the months of February and

March, and caused considerable disturbance in the social and commercial world. "Un étrange rhume rendit la voix si enrouée que les barreaux, les chairs et les collèges en furent amets." Mezeray also speaks of the great mortality among the very old: "Ce mal causa la mort presque à tous les vieillards qui en furent atteints."

In the works of Wolff[2] (p. 6) and Ruhemann (p. 7) I have found that mention is made in the report by the Bavarian ministry of war of *la grippe* in the German army in 1890,[12] of an epidemic in 1414, which is said to have occurred between Christmas and Easter in the Danubian District, and which was known under the name of *Bürzel* or *Tonawasches Fieber*.

Epidemic of 1427 (Ladendo).

This epidemic is mentioned by Gluge, Hirsch, and Ripperger, but the only authority upon which they rest is Pasquier. This writer repeats the description, given by an unknown author of that time, as follows: "L'an 1427 vers la S. Remy (October 1st) tient un autre air corrompu qui engendra une très-mauvaise maladie, que l'on appeloit Ladendo (dit un autheur de ce temps-là) et n'y avoit homme ou femme qui presque ne s'en sentit durant le temps qu'elle dura. Elle commençoit aux reins, comme si on eust eu une forte gravelle, en après venoient les frissons et estoit-on bien huit ou dix jours qu'on ne pouvoit bonnement boire, ni manger, ni dormir. Après ce venoit une toux si mauvaise que quand on estoit au Sermon, ou ne pouvoit entendre ce que le Sermonneur disoit par la grande noise des tousseurs," etc. Pasquier concludes with the words of his author: "Et s'entremocquoit le peuple l'un de l'autre, disant: As-tu point eu Ladendo?"

We have before us, therefore, as seen above, quite a characteristic description of this disease. The symptoms consisted in pain in the kidneys, chilliness, anorexia, insomnia, and cough. A proof of its great distribution is also found in the question people habitually put to each other during the epidemic: "As-tu point eu Ladendo?"

We will pass over the epidemic of 1438, which visited all Italy as a catarrhal desease (cited by Zeviani), and was equally dangerous to children and old persons. Also the epidemic of the year 1482, for which Zeviani cites Mezeray, whose inexact description consists in the following: "Il courut une maladie épidémique toute extraordinaire, qui attacquait aussi bien les grands que les petits."

Epidemic of 1510 (First Pandemic).

The year 1510 is of especial importance in the history of influenza, as we here meet with the pestilence for the first time as a pandemic disease. The disease was spread all over Europe. It was brought, says Thomas Short (in Thompson's "Annals"[4]), to Sicily from the Island of Malta, then invaded Spain, Italy, crossed the Alps to Hungary, Germany, France, and England. Webster and Hancock also report that the epidemic originated in Africa. Thompson in England, and Saillant[5] in France, both begin their historic monographs with this epidemic, which is spoken of in Thompson's work in the following manner: "The first visitation of the disease in the British islands, of which we possess an accurate description, is that of the year 1510."

All historians of the disease, Zeviani, Webster, Schweich, Gluge, Thomas Short, Hirsch, Ripperger, Leichtenstern, and others, believe this epidemic to have been influenza; of other older writers, Valleriola, Fernelius, Johannes Schenk, A. Grafenberg, and Mezeray may be mentioned.

Valleriola speaks of an epidemic catarrh which visited France in 1510, and was said to have been similar to the epidemic of 1557. Fernelius, physician to Henry III. of France, writes: "Communis illa porro omnibus decantata gravedo anhelosa anno 1510, in omnes fere mundi regiones debacchata, cum febre, cum summa capitis gravitate, cum cordis pulmonumque angustia atque tussi, quamquam multo plures attigit quam jugulavit."

Saillant (p. 4) says: "En 1510 régna en France une fièvre catarrhale épidémique. Les médecins la regardèrent, dit Schenkius, comme une maladie nouvelle." Zeviani quotes from G. Hors: "Huc etiam pertinet ruatum epidemium (?) gravedo scilicet anhelosa cum tussi quæ ante 90 annos universum fere mundum ab occidente in orientem per omnia quatuor anni tempora pervagata."

Thomas Short says concerning the wide distribution of the disease throughout Europe: "The disease . . . attacked at once, and raged all over Europe, not missing a family and scarce a person."

Zeviani's reference to de Thon concerning the epidemic of 1510 is an error, which is repeated by Ozanam and Schweich and was discovered by Gluge.

The symptoms of the disease mentioned in the chronicles of this epidemic were fever, cough and hoarseness, headache, anorexia, and insomnia, also pains in the stomach, kidneys, and legs (Bouchet[13]). The character of the epidemic was benign.

Fernel says, "Multo plures attigit quam jugulavit." Thomas Short, "None died except some children." Mezeray, on the other hand, remarks that the disease had claimed many victims.

The names given to the disease in France were cephalie catarrhale, toux catarre, coqueluche (obligé de se couvrir la tête d'une coqueluche ou coqueluchon—Saillant); in England, coccoluche or coccolucio (because the sick wore a cap or covering close to their heads—Short).

Epidemic of 1557.

The epidemic of 1557 also extended over the whole of Europe. According to Hirsch (p. 6) it invaded Sicily in the month of June, Italy in August (Padua, Lombardy), Dalmatia, Switzerland, and France in September (Poitiers, Montpellier, and Nîmes), and in October, the Netherlands (Harderwyk and Alkmaar) and Spain. Gluge and Hirsch speak only of the spread of the epidemic in Europe. According to Thompson's "Annals" the epidemic invaded Europe by way of Asia, from Constantinople, and then also extended to America. Hermann also asserts, without giving us his authorities (Ripperger), that the pestilence appeared in America. We are indebted to Pasquier again for some very interesting statements; he says (p. 375): "Tout ainsi [referring to the epidemic of 1403] que nous vismes en 1557 en plain esté s'élever par quatre jours entiers un rhume qui fut presque commun à tous; par le moyen duquel le nez destilloit sans cesse comme une fontaine, avecqu' un grand mal de teste et une fièvre qui duroit aux uns douze, et aux autres quinze heures, que plus que moins puis soudain, sans ouvre de Médecin, on estoit guery. Laquelle maladie fut depuis par un nouveau terme appellée par nous Coqueluche."

Riverius (p. 585) repeats the description of an anonymous physician, who wrote that in the month of July, 1557, the city of Nîmes was invaded by an epidemic disease called coqueluche. The disease, which spared no one, was cruel; most persons attacked by it were taken off, some on the fourth, others on the seventh, still others on the fourteenth day of illness. The main symptoms were an exceedingly distressing cough and a violent, continuous pain in the kidneys.

Valleriola describes the enormously wide distribution of the epidemic throughout the whole of France; it appeared with pestilential rapidity, and spared neither sex nor any age nor rank, neither children nor old persons, rich nor poor, but it was not as a general rule dangerous, children only, who could not freely cough out the phlegm, dying.

In contrast to this, Coyttar" speaks of the benign character of the

epidemic; it was widely disseminated, but with the exception of some phthisical patients there were no deaths. "Ut vix e millibus unum invenias qui non eo tempore coccelucha laborarit. Quam tamen non usque adeo periculosam aut crudelem fuisse existimes vellem, ut credas multis exitio fuisse, cum certe neminem hominum (quod sciam) viderim qui hoc symptomate gravatus satis concesserit."

Thomas Short reports upon this epidemic in England: "It was a very unseasonable year in England. . . . In the end of September came a very strong cold north wind, presently after were many catarrhs, quickly followed by a most severe cough, pain of the side,* difficulty of breathing, and a fever. The sixth, seventh, or at the farthest, the eighth day, all who had that pain of the side died." Short also gives a very good description of the epidemic in Spain: "At Mantua Carpentaria, three miles from Madrid, the epidemic began in August. . . . There it began with a roughness of the jaws, small cough, then a strong fever with a pain of the head, back, and legs. Some felt as though they were corded over the breast and had a weight at the stomach, all which continued to the third day at furthest. Then the fever went off, with a sweat or bleeding at the nose. In some few, it turned to a pleurisy or fatal peripneumony."

Forest reports from Holland (Alkmaar) that the epidemic made its appearance with considerable violence there in October. The disease came on very suddenly, "quodam affluxu," so that one thousand persons were attacked at the same time. Forest still further observed that abortions were frequent during the epidemic, so that sixteen women died of this cause within eight days.

Short also mentions the epidemic in Holland. He says: "This disease seized most countries very suddenly when it entered, catching thousands the same moment." The main symptoms, besides violent headache and tormenting cough, were severe dyspnœa ("that the sick seemed dying"), accompanied by pain in the loins on walking, "constant severe pain of the loins that they could not walk" (Riverius[20]).

As regards the season of the year, the influenza occurred in Paris during the hottest part of summer (Pasquier), in the city of Nîmes in the month of July (anonymous, in Riverius), in Spain, Mantua Carpentaria, in August (Short), in England in September (Short), in Holland, Alkmaar, in October (Forest and Short).

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* Dodonaeus also speaks of pains in the side which, when they became severe, necessitated a bleeding.

Epidemic of 1562 and 1563.

We shall omit the year 1562, in which Ripperger speaks of an epidemic, the existence of which he tries to prove from the contents of a letter written by the English ambassador Randolph to Lord Burleigh, dated November 30th, 1562, rejecting the authorities cited by Hirsch for Italy.

The epidemic of 1563 we shall also mention only briefly. It was reported to Gessner in a letter by Johannes Bauhin, who was himself a victim of the disease: "Gravitas capitis cum dolore et defluxionibus magnis, quibus correpti sumus fere omnes; vocant hunc morbum Galli coqueluche."

Biermer pronounces the disease influenza, Ripperger agrees with him; Gluge does not mention it, and neither does Hirsch nor Leichtenstern. Zeviani (p. 481) mentions the letter of Bauhin to Gessner as written in 1562; and he says nothing of an epidemic in 1563. Whether influenza occurred in 1562 and 1563 is undecided; at all events, providing our sources are complete, there were only small epidemics in those years.

Epidemic of 1580 (Second Pandemic).

As in 1557, an epidemic of influenza again swept over the earth in 1580, only to much greater extent. According to Hirsch (p. 6) it covered the whole Orient as well as Africa and Europe. Cesare Campana in his "Istoria del mundo," states that it was distributed not only over Europe, but also over Africa and Asia, and Suan also tells us that the epidemic invaded both hemispheres. Lastly, we have a report from Fonseca which tells us that the epidemic extended from Asia by way of Constantinople over the whole of Europe, and that it afterwards also visited America.

According to Pechlin,[15] the disease made its appearance first in Africa and on the Island of Malta, from whence it was carried into Sicily, then to Spain and Italy, crossing the Alps to Pannonia, Hungary, and Germany, as far as the Baltic Sea. Johannes Bockell[16] describes its march as follows: "Primo Hungaros, Panonas, Bohemosque vicinos, post Francos Thuringosque invasit, Belgas Brittanosque."

According to Short the epidemic prevailed "over all Europe," and with especial virulence in England, from the middle of August to the end of September, returning again in October and November of the same year. Towards the middle of the year we find the influenza

present in France (Lobineau), where, according to a writer quoted by Saillant, it broke out immediately after a visitation of swarms of insects which appeared during the months of April and May in extraordinarily large numbers. Coyttar observed this epidemic in the month of May at Poitiers. In Naples the influenza occurred during August and September (summonte), and visited Campana in the same year, "per tutta Italia." Germany suffered from the epidemic of this year late in the summer and in the autumn; according to Hirsch (p. 6) in August Augsburg, in September the neighborhood of the Rhine, Helmstadt, and Silesia, in October Saxony and the shores of the German Ocean. Sennert reports that it devastated Germany from the end of summer to the beginning of autumn. In the history of this epidemic we already find mentioned, besides the usual symptoms, such as headache, cough, hoarseness, angina, fever, and chills, physical weakness, pains in the muscles and joints, anorexia, insomnia, gastric catarrh, diarrhœa, delirium, pain in the chest, and dyspnœa—also numerous complications, especially otitis, parotitis, and affections of the bile-ducts, from which was derived the name of "catarrhus biliosus," used by some.

Bokel says: "Experientia quoque didicimus ad aures ex tussi . . . materiam concitatam pluribus defluxisse." The frequent appearance of otitis is well known to us from our recent influenza epidemics; in truth, we learn from all these descriptions that this epidemic corresponds fully with our own influenza epidemics, with the exception only that individual observers report an enormous death-rate. Thus, according to Schenkius, the disease killed nine thousand persons in Rome; Madrid, Barcelona, and other Spanish cities are said to have been nearly entirely depopulated by the disease (Villalba[21]). This high mortality was, however, even at that time attributed by some physicians to the injudicious employment of venesection. Wierus[22] says that out of one thousand persons hardly one died, except those who were already previously afflicted with some chronic disease, or "qui venæsectione usi sunt." Crato[23] says further: "Eventus ostendit, graviter illos periclitatos—et literis ex Hispania missis perscriptum est, supra duo millia hominum, quibus in unica urbe Mantua Carpentaria sanguis fuit detractus intra paucos dies obiisse." Mercatus[24] also testifies that the Spanish physicians bled many patients, which usually led to their death. Sennert (quoted by Saillant) says the same of Italian physicians. They were, to use Saillant's words (p. 11): "Trop prompts à tirer le sang; car l'expérience, ajoute-t-il (that is Sennert), a prouvé que presque tous ceux dont on avait ouvert la veine, étaient morts." Short says (p. 9): "Though all had it, few died in these countries except such as were let blood

of, or had unsound viscera." Others also condemned the letting of blood, among them Bokel, according to whom most patients recovered without any medicine (plurimi sine pharmacis ad sanitatem edierunt). Similarly Mezeray says: "Elle se montrait plus douce à ceux qui la laissaient en repos."

The complications mentioned by Short are "consumption, pleurisy, and peripneumony"; and Bokel says "hic morbus in peripneumoniam periculosam et phthisim lethalem transiit."

It may be mentioned in passing that Anna, the wife of Philip I. of Spain, died in the epidemic of the year 1580, and that the king himself, and also Pope Gregory XIII. had the disease in a dangerous manner. For this information we are indebted to de Thon, but the event was wrongly placed by Zeviani under the epidemic of 1510. This mistake of Zeviani was propagated by Ozanam and Schweich, was corrected by Gluge, but has again made its appearance lately in the work of Zuelzer.

Epidemics of 1591, 1593, and 1597.

In the close of the sixteenth century Hirsch also mentions as epidemic years 1591, 1593, and 1597. Of these three we can accept only one, that of the year 1593.

Sennert described the epidemic of 1591 in Germany. It was, however, somewhat different from that of 1580; Tansonius described it in Italy, calling it an "épidémie cruelle," adding that "presque tous le malades tombaient dans un délire frénétique et mouraient le huitième ou le dixième jour." The severe nervous symptoms, especially the malignant character of the disease as evidenced in the great mortality (in Rome sixty thousand persons were said to have died from it within a year) speak against influenza. Cagnatus described the epidemic of 1591 in Rome; that it was not one of influenza can be seen from the beginning of the description: "Cæperunt Romæ apparere febres acutæ et his præcipue notis insignatæ, maculæ in cute verbentes," etc.

According to Hirsch, the disease is said to have invaded Italy in September, 1587. Zeviani refers to Schenckius, who had been informed by letter from friends that more than nine thousand persons had perished by the pest in Rome, at the time when Germany was also visited.

Of the influenza epidemic of the year 1593, we are in possession of reports, besides those of Chifflet and du Laurens, from Marsilius Cagnatus[26] who describes the epidemic in Rome. The symptoms at this time were fever, lasting at most four days, headache, cough, angina (inflammation of the throat), hoarseness; the headache is said

to have appeared frequently after the cough. The greater number recovered, it is said, by taking food only in moderation. The physician was not, as a rule, frequently consulted, for "res visa levis et citra periculum"; only a few fared badly. "Aliquibus desiit in pleuritidem lethalem, sed maxima pars sanitati restituebatur."

As to the spread of the epidemic Cagnatus (p. 59) says: "Cum aliquis primo in numerosa familia ægrotat, in eadem paucis post diebus multi eodem febris genere capiuntur." Thus it happened that the disease which made its appearance "after the Ides of June," had already attacked the greater part of the people in the beginning of July.

The epidemic is said to have commenced in Belgium, following a "violent earthquake," and gradually extending over all the cities of Europe.

Epidemic of 1626.

Gluge says that this epidemic is probably to be looked upon as one of influenza. Later authors accept it without any doubt. Ruhemann, it is true, has found it only in Gluge. We possess a good description of this epidemic by two authors, namely, that of the Italian physician, Paulus Zachias, cited by Zeviani (p. 485), and that of Donius, both describing the disease as it occurred in Italy.

Paulus Zachias says: "Nam et benignissimi quidam vagantur morbi populares, quales sunt raucedines et gravedines quæ hoc tempore plures Italiæ urbes molestaverunt et adhuc anno presenti 1627 molestant."

Donius writes: "Anni vero 1626 recens est memoria cuius ingressus atque initium hiemis perniciem plurimis non hic Romæ tantum sed toto fere Italia conflavit, ob vehementer enim Borcæ flatus qui subito Austrinos dies eosque perhumidos exceperunt multas destillationum pravas ac noxias species incitavit quam ridiculo nomine Castrone vocant."

Epidemic of 1647.

Webster gives us the information that in this year influenza is for the first time mentioned in the history of America; but we must not argue from the absence of earlier histories that influenza never before occurred there. Webster cites the following from Hubbard's description of this disease: "It began with a cold and in many cases accompanied by a light fever. Such as bled or used cooling drinks died; such as made use of cordials and more strengthening things recovered for the most part. It extended through the plantations in America and in the West Indies; there died in Barbadoes and St. Kitts five thousand or six thousand each."

Epidemic of 1658.

This is one of the best described influenza epidemics, although its literature is not voluminous. According to Wittmer, its description tallies exactly with the influenza pandemic of the year 1782. We are in possession of a very well-written description by Thomas Willis of Oxford, which can be found in Thompson's "Annals" (pp. 11 and 12); it says: "About the end of April, suddenly a distemper arose, as if sent by some blast of the stars, which laid hold on very many together, so that in some towns in the space of a week, above a thousand people fell ill together." Then follows the enumeration of symptoms: Troublesome cough with copious expectoration, catarrh of the nasopharyngeal space, fever with heat and thirst, anorexia, malaise, pain in the back and the limbs, occasional nosebleed, bloody expectoration, and bloody stools. The disease affected some very lightly, so that they were able nevertheless to attend to their business; others, however, and particularly debilitated persons and old people, were rapidly taken off by it.

Timæus von Güldenklee,[27] who observed this epidemic in January, 1658, at Treptow near Stettin, and who was himself attacked by it, is our second authority. In a letter to his brother he makes a comparison with the epidemic of 1580, writing thus: "Dubium mihi non est, frater meus, quin cum mille morbis conflicteris, secustamen atque ego cum catarrho epidemico simili fere, quorum auctores sub anno 1580 referunt febrilemque nominant." He suffered from the following symptoms himself: Fever, very violent cephalalgia, cough and expectoration, great pain in the chest, the side, and the diaphragm, insomnia, and attacks of perspiration at night. The disease came on very suddenly.

Epidemic of 1675.

The epidemic of this year visited Germany during the month of September, and was greatly disseminated, for no house, says Rayger, was spared, and each contained one to four patients. In October it had reached Hungary and at the same time Austria, where Sorbait [28] observed it in Vienna.

In England, where it broke out in London towards the end of October, it found a historian in Thomas Sydenham (Thompson's "Annals" [1]). The latter reports that in the year 1675, after clear weather had obtained to the end of October, a frost suddenly appeared, which brought with it a greatly disseminated coughing sickness. "No one escaped them, whatever might be his age or temperament, and they

ran through whole families at once." Together with the cough there was present fever, headache, pain in the back and limbs. As complications are mentioned affections of the lungs and pleura, so that some thought of pleurisy or peripneumonia, but in Sydenham's opinion wrongly so, for "yet it was neither more nor less than what it had been throughout. Now, as before, it attacked with pain in the head, back, and limbs."

In France the epidemic exerted a very unfavorable influence on pregnant women. Bloody expectoration, according to Sorbait, was of frequent occurrence in Vienna, "plurimi sputo sanguinis laborabant Viennæ." Ettmüller, to whom we are indebted for a minute description of this epidemic, informs us that the breathing occasionally became so oppressed that death seemed imminent. The cause of the epidemic was ascribed by him to the air, which attacked the glands. As to the character which the epidemic presented, no one died, according to Rayger and others, from the disease itself, with the exception of debilitated persons, although it spared neither the strong nor the weak. Willis succumbed to the disease.

Epidemics of 1688 and 1693.

According to Hirsch, there were two influenza epidemics occurring in the years 1688 and 1693, for which he only mentions one authority, namely, Molineux.[3] Ripperger also is convinced that the epidemics of 1688 and 1693 were influenza, while Gluge accepts as certain only the epidemic of 1693.

The epidemic of 1688 brought with it a great mortality in England and Ireland. It made its appearance in London in May, extended during this and the following month all over England, and in the month of July also over Ireland. Short writes (Thompson's "Annals," p. 24): "We find that at the middle of May began a fever in London all over England, and all over Ireland in July. The symptoms were the same in all. It began and ended its course in seven weeks. . . . Though not one of fifteen escaped it, yet not one of a thousand that had it died."

At the same time there is this said of an epizootic occurring in the same year: "It was generally observed, both in England and in Ireland, that sometimes before the fever began a slight but universal disease seized horses, viz., a great defluxion of rheum from their noses" (cf. the Epidemic of 1404).

In the year 1693, in the early part of November, influenza broke out in Dublin, and so very general did this influenza prevail, that few or none escaped. It also invaded Oxford. It made its appearance

in London about one month later than in Ireland. It also invaded Holland and Flanders (Molineux).

The symptoms were a violent cough, a great flux from the nose and eyes, hoarseness, angina, pain in the chest. A cure usually occurred spontaneously, with a critical sweat.

"All conditions of persons were attacked, those residing in the country as well as those in the city; those who lived in the fresh air and those who kept to their rooms; those who were very strong and hardy were taken in the same manner as the weak and spoiled; men, women, and children, persons of all ranks and stations in life, the youngest as well as the oldest" (Molineux, p. 106). Molineux, however, thinks that very old people were relatively less frequently attacked by the disease, for he says: "It rather favored the very old, who seldom were attacked with it."

Epidemic of 1709.

There were many epidemics in the eighteenth century, but we shall dwell only on the most important. The epidemic of 1709 visited, it is said, Italy, France, Belgium, Germany, and Denmark (Hirsch). Its historians were Lancisius,[30] Hoffmann,[31] and Bianchi[32] and from these we glean, as a general rule, but little of the epidemic. Gluge denies that the epidemic of this year was influenza, on account of the simultaneous invasion of Berlin and Italy and also on account of the symptoms as described by Ramazzini. We know from Lancisi, however, that the epidemic existed in Italy in January, and from Hoffmann that it did not make its appearance in Berlin until April, and thus the first objection of Gluge is answered. Gluge's second objection, that the prisons of the inquisition, which on account of the lime kilns present in their vicinity, had a higher temperature, remained free, according to Lancisi, from influenza, and also that persons who had no occasion to expose themselves to the fresh air—for example, women, wealthy people, etc.—were relatively less frequently attacked by the disease, is not sound, for in later influenza epidemics similar observations have been made. Moreover, Lancisi himself believes the disease to have been influenza, that is, identical with the epidemics described by Cagnatus (1593) and Donius (1626).

Bianchi compares the epidemic of 1712, which is universally acknowledged, with that of 1709, a fact which also speaks in favor of this being influenza.

The following complications are reported by Hoffmann: An itching exanthem, on the fourth day, similar to urticaria; rheumatic

pains, especially in elderly women; relapses in those who did not remain indoors long enough; and purulent expectoration and a bloody cough (sæpe vera phthisis) in those having lung disease.

The scorbutic eruptions, described by Hoffmann, do not fit the picture of the disease altogether (he speaks of maculæ rubræ et asperæ in extrema cutis), although in the last epidemic of influenza, it is true, complications with purpura hæmorrhagica (Drashe, Senator, Ewald) and with erythema papulosum (Hawkins) have been observed. Zeviani also makes mention of this epidemic in Prussia, and cites Hoffmann.

Ripperger (p. 47) believes the epidemic of 1709 to have been influenza without a doubt, and following him, Gluge only denies it recognition because it did not travel from east to west, which, according to Gluge, was the case with all influenza epidemics from the end of the sixteenth century.

Epidemic of 1712.

This was carefully described by a number of observers, especially by Camerarius" and Slevogt," as also by Schröck and Waldschmidt in Germany, by Bianchi in Italy. The observers of this epidemic all agree as to the rapidity of the attack, as well as to the great debility which accompanied the disease. The morbidity was very great. According to Schröck, not a house was spared by the disease in Augsburg, Waldschmidt tells us that in Kiel ten and more persons were frequently taken ill in one house, and Slevogt says that the disease was fearful, because so many persons contracted it at the same time. The disease was, however, not dangerous, for Slevogt continues: "Fear soon vanished when it was seen that although it had spread all over the city, it left the sick with equal rapidity," and Camerarius is of the opinion that if the disease had been as dangerous in the same degree that it was disseminated, the world would never have experienced a greater misfortune. Bianchi compared this epidemic with that of 1709 and pronounced the latter more violent, and the words he uses, "multi ægrotabant pauci vero interibant," are significant of the character of the epidemic of 1712.

As regards the symptoms, Camerarius in his description emphasizes the following: "As a general rule those suffered most who had previously been sickly, nevertheless those also who were strongest and believed they could resist the disease, had to give in and were vanquished." As a general rule there were present: fever and an accelerated pulse-rate, occasionally accompanied by all kinds of phantastic illusions and dreams; coryza, hoarseness, cough, a feeling of oppression; headache, pain in the eyes, pain in the back, in the

loins, in the limbs, as in "dem förmlichen Gliederweh;" anorexia, nausea, eructations, and diarrhœa.

The epidemic began in Germany: Jena in the spring (Slevogt, Lanzoni); Holstein in July (Waldschmidt); Augsburg in August (Walderschmidt, Schröck); Tübingen in September (Camerarius); in Holland in August; in Italy in December (Bianchi).

Epidemic of 1729–30.

This is the first epidemic of which it is said that it originated in Russia, although according to Loew[35] the influenza of this year came from Sweden, and F. Hoffmann claims to have already observed it in February of 1729, at Halle. According to Buchner[36] this epidemic was said to have all at once, and suddenly, broken out in Moscow in the middle of the month of April, 1729, so that the imperial court had to flee from the pestilence to a pleasure palace situated thirty miles from Moscow. From Russia the disease then spread over the whole of Germany, Austria, England, France, and finally over Italy, where the epidemic reigned during the month of March, 1730, and, as we see by the records, also ended here.

Its morbidity was again enormous, the rapid lightning-like appearance of the epidemic is frequently alluded to. In Rome it is estimated that sixty thousand people were stricken with it, in Mayence fifty thousand, in Turin fourteen thousand; in London barely one per cent. escaped. In Lausanne one-half of the inhabitants, then estimated at four thousand, sickened. In Vienna the pestilence suddenly broke out on the 21st of November, and over sixty thousand persons were affected; and in the monasteries of Paris there were so many of the inmates ill from influenza that no services could be held.

Pelargus[37] says: "From November 16th to the end of the month the route was greatest, as it also involved the medical men to such a degree that we were within two days reduced in a body to the condition of the laity," from which it may be seen that the physicians also were compelled to take their share of the fate of the general public.

This picture of influenza, which has been carefully described by all recorders, with its catarrhal, nervous, and gastric symptoms, permits of no doubt as to its genuineness.

The great mortality which attended the epidemic in England and Italy seems somewhat remarkable. Thus Hahn states that in London in the month of September, one thousand persons died each week, and in Mayence forty persons daily. Most likely, however, other diseases which were present at the same time added their quota to the

mortality, especially as the disease in other places, for example in Germany, ran a benign course.

Pelargus writes as follows of those few that died with the influenza (he claims to have lost by death in October only six out of one hundred and forty-five patients): "Although nearly all these patients had carried death with them for some time, and some could only have lived a few months, I do believe that they would not have died in this month if the febris catarrhalis epidemica had not thrown its weight against them, from which it is especially to be remembered that these fevers, when they attack consumptives or such persons as are somewhat weak in the chest, usually become dangerous."

The complications mentioned as occurring in this epidemic were phthisis, pneumonia, pleuritis, inflammation of the brain, delirium, convulsions, petechiæ, miliaria, parotitis, and abortion.

The epidemic appeared in April, 1729, in Moscow and Astrakhan; September, in Breslau and Sweden; October, in Silesia, Vienna; November, in Eisenach, Wittenberg, Nuremberg, Regensburg, Riga, London; December, in York, Vienna, Paris, Zurich, Luzerne; January, 1730, in Lausanne; February, in Rome and along the Rhine; and March, in Naples. According to Hirsch, influenza appeared for the first time this year in Iceland.

Epidemic of 1732–33.

This epidemic was spread over the entire earth, as we learn from evidence recently brought forward showing that it also occurred in America. If the statements of Perkins[3] are correct, the epidemic had its beginning in October, 1732, in Connecticut, invaded Massachusetts the following day, and appeared at Annapolis two days later, where it attacked half the garrison, and broke out two days later in Newfoundland. It then travelled, according to the Edinburgh "Essays,"[3] to the West Indies (Jamaica, Barbadoes) and Mexico, as well as to South America (Peru, Chile). Webster[1] writes as follows: "Towards the close of the year, in October, commenced in America a severe universal catarrh, which appeared in Europe also in December. It spread over all Europe in the beginning of 1733, and probably over the earth, as it was experienced at the Isle of Bourbon in the Indian Ocean."

Pelargus informs us that the epidemic came in November from Russia by way of Poland to Germany (Thuringia). It then spread in this and the following month over the whole of Germany, over Switzerland, Holland, England, and Scotland (Edinburgh). In January, 1733, it made its appearance in France, in February in Spain

and Italy. As descriptive of these epidemics the sentence "great morbidity with a relatively small mortality," may also be applied.

Huxham applied the term "morbus omnium maxime epidemicus," to the disease. In Thomson's "Annals" he is quoted as affirming that "not a house was free from it, the beggar's hut and the nobleman's palace were alike subject to its attack, scarce a person escaping either in town or country, old and young, strong and infirm, shared the same fate."

Pelargus treated during the month of October 10 patients with influenza out of a total of 27; in November, 155 out of 162; and in December, 380 out of 410. The disease was not dangerous, as we learn from the almost unanimous testimony of the historians of this epidemic, such as Perkins, Huxham, Pelargus, Carl, and others.

The following complications are mentioned: Pleuritis, pneumonia, phthisis, parotitis, orchitis, swelling of the salivary glands, earache, abscess of the ear, miliaria, petechiæ, and herpes labialis.

Réamur,[40] in describing influenza as it occurred on the Island of Bourbon, east of Madagascar, says that vessels on the open sea were attacked by the disease.

Epidemic of 1737.

This is not generally recognized as a visitation of genuine influenza. Hirsch mentions as his authorities Huxham and Webster, and mentions Plymouth, in England, North America, Barbadoes, and France as the regions invaded. Webster says only: "In 1737 a very severe influenza invaded both hemispheres. It commenced in November," while Huxham gives a good description, fitting influenza very well, although Gluge says of it that it does not warrant the belief that the disease was influenza. Speaking first of the great spread of this disease, which latter was not dissimilar to that of 1733, Huxham mentions as symptoms particularly hoarseness, headache, pain in the back and loins, oppression, fever, angina; we again find the following remark by him: "Sæpius vero faciei tumor parotidum maxillarum secuta est."

Epidemic of 1742–43.

In the accounts of this epidemic we find for the first time the names influenza and grippe, designations which the disease has retained to the present day.

Although the word "influenza" is undoubtedly of Italian origin, especially as the Italian chronicles (according to Zeviani and Gluge) in all epidemics speak of "una influenza di freddo," this name was first used in this epidemic in England, and nearly all authors mention

the English physicians Pringle[1] and Huxham[2] as the originators of the name.

As regards the Italian word influenza Biermer[3] observes: "We wish to call attention to the fact that influenza in Italian does not only mean flux, but also something fluid, temporary, the fashions and therefore also a temporary pestilence, a disease of fashion." The same author furthermore says (*ibidem*): "In France the 'influenza' has generally been called la grippe, since the epidemic of 1743. This designation is probably derived from agripper (to attack), and not likely from the Polish word chrypka (raucedo), as T. Frank believes." According to Most the word influenza (from influere, to flow) was used to designate that the patient was attacked by "some unknown influence."

Speaking of the epidemic itself, it may be stated that it first appeared in single cities in Germany, thus in January at Coburg, in February at Dresden and Coblenz. After this it is not again mentioned until the spring, when it appeared anew in Switzerland, to invade from here during the winter of 1742–43 the whole of Italy. It then passed to France, Holland, and Belgium. In April it visited England.

The epidemic was marked by an enormous morbidity where it reigned, but the disease was not dangerous as a general rule, although Huxham occasionally speaks of the virulent character of the epidemic in England, and Cohansen says that in January, 1743, over eight thousand persons died from influenza in Rome and five thousand in Mayence.

The following complications were mentioned: "Inflammation of the lungs with extraordinary dyspnœa and bloody sputum, which frequently, particularly in old persons, ended in death" (Gluge); purpura and exanthemata of the cutis, "multæ rubræ urentes pustulæ" (Huxham). The great mortality mentioned by Huxham and Cohansen for England and Italy is attributed by Cullen to the abuse of venesection in these countries.

Epidemic of 1758.

Concerning the epidemic of this year, in which the influenza invaded France and Scotland, there are extant only a few records. Hirsch claims that this epidemic was widely spread throughout North America, alleging as his authority Webster, in whose works, however, nothing can be found relating to this epidemic. Hillary says only that in September, 1757, the influenza had invaded the island of Barbadoes.

In the month of May, 1758, the epidemic made its appearance in the French capital and in Lille. Our best records are those from Scotland. Robert Whytt (Thompson's "Annals," p. 61) writes in a letter to Dr. Pringle that the disease had arrived in Edinburgh and vicinity towards the end of September, and spread more and more in that locality during the early part of October. "Old as well as young were taken ill; nay, even women in childbed, who were not exposed to the cold air, were affected."

On October 24th, Whytt continues, the pestilence began to abate. He is not sure whether this was due to a change in the weather, or because the disease had already attacked most people, although the latter seems more plausible to him, particularly as he says that "in Edinburgh and its vicinity not one out of six or seven escaped," and in other localities it is said to have been even worse. In the north of Scotland also, the epidemic was greatly disseminated from the middle of October to the end of November. A young physician wrote to Robert Whytt: "It was the most universal epidemic I ever saw, and I am persuaded that more people were seized with it than escaped." This same physician reported that "it was not at all mortal here."

Whytt mentions that the disease became more dangerous towards the end of October and the beginning of November, "by falling on the lungs, pleura, muscles of the thorax."

It should be mentioned that Whytt gives us with this epidemic also news of an epizootic. Before the influenza broke out, there existed in September a disease among horses, in Perthshire. "The horses were observed to be more than usually affected with a cold and a cough." Whytt did not believe the influenza contagious, and neither did he believe that the air was the cause of the epidemic, as the season of the year was a mild and dry one.

Epidemic of 1761.

According to Webster, the influenza visited America in this year, for he says in regard to the year 1762 that the influenza made its appearance in Europe one year later than in America.

The influenza appeared in the spring of 1761 in the northern parts of America. In Philadelphia it occurred in the winter (Webster probably means the winter of 1760–61), in Massachusetts in the month of April, in the same month and also in May in Weymouth; it even reached the West Indies in its march "through the whole country," having invaded Barbadoes in May.

As symptoms are described: a severe pain in the head and limbs, sensation of coldness, shiverings succeeded by great heat, running at

the nose, troublesome cough. The duration of the attack was usually eight to ten days, and it ended with a sweat (Webster).

Epidemic of 1762.

This was, according to our records, nearly general throughout Europe, appearing first in Germany—namely, in February at Breslau (Hancock [4]), in March at Vienna, in April at Hamburg, Magdeburg, and Bremen; it had already visited Hungary and Denmark. According to Watson (Thompson's "Annals," p. 76) the influenza appeared at London and its neighborhood in the beginning of May and remained there during the whole of May and a part of June. Ozanam [4] curiously interpreted the word neighbourhood or "heighbourhood" as he has it as the name of a locality, and accordingly writes: Watson, . . . "dans une lettre à Huxham . . . décrit cette épidémie, qui regna à Heighbourhood."

The pestilence also visited Ireland, where it was "severe and general" in Dublin in May, also Scotland, where the first few cases appeared in Edinburgh in the month of April. In June, Strasbourg and all of Alsace were attacked. In the middle of July the influenza took possession of Nîmes, "où elle n'enleva que très-peu de personnes" (Saillant [4]), in the same month British sailors sickened with it on the Mediterranean Sea, and in September and October it was still present in a number of provinces of France. The influenza of this year was very irregular in its appearance, however, being reported now here, now there, without any apparent sequence.

Regarding its great morbidity we have reports from Razoux and de Brest, and testimony as to its low mortality is furnished also by Razoux, Saillant, and Ehrmann. According to Mertens only asthmatic old persons and consumptives died.

No new complications are reported in this epidemic, except abortions and premature births, which are mentioned by Baker.[4] Pleuritis and pneumonia are also mentioned in Thompson's "Annals" (p. 72), which, however, are said to have attacked those persons who would not take to their bed early.

Razoux mentions the names *la baraquette, la grippe, la petite poste, le petit courier*, as new designations for influenza in France.

Epidemic of 1767.

Influenza is said to have appeared, according to Gluge and Hirsch, who both refer to Perkins, not only in Europe but also in North America in the month of May, 1767. Webster, however, does not mention an influenza occurring in America in this year.

It first appeared in Germany in April, 1767. In Eisenach nine-tenths of all the inhabitants contracted the disease (Grimm"). In the beginning of June the first cases of sickness appeared in London, by the middle of the month it had become epidemic, reaching its height in the last week of June and the beginning of July, and had disappeared by the end of July.

France was visited by the influenza in the months of July, August, and October. In the latter month as well as in November it appeared in Italy, in December in Madrid and the whole of Spain, where it was described by Villalba[31] who states casually that this epidemic had travelled over the whole of Europe in a period of two months.

The year 1772 is designated by Hirsch, also by Hauser, Hermann, and others, as an influenza year, but Webster says that in February, 1772, there prevailed in all parts of America an epidemic catarrh, which was attended or followed by measles of unusual malignancy. In Charleston, S. C., eight hundred or nine hundred children died. We are justified, therefore, in erasing the year 1772 from the history of the influenza.

Epidemic of 1775–76.

This invaded Germany, Italy, England, Ireland, and France successively, from March, 1775, to January, 1776, and seems to have had its origin in Germany; we are in possession at least of information that the influenza made its appearance in the autumn of 1775 in the village of Clausthal, in the Harz Mountains. In June it had invaded Vienna. From June to September it is not mentioned, but in the latter month it again made its appearance in Italy. In the months of October, November, and December the influenza broke out in England as well as in France, and in the latter country it was still present in January, 1776. The most accurate information which we possess of the epidemic of this year comes from England, namely, in the medical observations and inquiries by a society of physicians in London (Thompson[4]). There were altogether sixteen reporters; of these, five physicians in London give us a record of the epidemic.

According to Fothergill the disease originated in London in the beginning of November; old asthmatic persons suffered most. He said that he had no knowledge of any other example of an epidemic disease "where so many persons were seized, and in so short a time, and with so little comparative mortality." Mention is also made of an epizootic: "Horses and dogs were much affected, the horses had severe coughs, were hot, forebore eating." Sir George Baker says that the epizootic probably began a few days before the 20th of Octo-

ber. He did not always meet with the white tongue of which Fothergill speaks.

Heberden says that no one died of the disease, but he adds that "it seemed to hasten the death of two or three persons whom it found dying of age and other disease."

Thomas Glass speaks of the appearance of the influenza in institutions: "There sickened in the Exeter Hospital all the inmates, one hundred and seventy-three in number; one hundred and sixty-two had coughs. Two or three days after the hospital was invaded the city workhouse was attacked; of the two hundred paupers housed there, only very few escaped the disease."

Pulteney, of Blandford, says that the influenza was present there before it visited London. He praises the good effects of venesection, as a result of which he thinks none died of the disease. He adds concerning an epizootic: "I heard much of horses and dogs having been affected, before we heard of it among the human race."

Daniel Rainy, of Dublin, reported the invasion of an institution by the influenza. It gained an entrance to the House of Industry which contained at that time about three hundred and sixty-seven persons, varying in age from twelve to ninety years. Of these three hundred and sixty-seven inmates two hundred were taken sick.

The following complications are mentioned in the accounts of this epidemic: Swelling of the tonsils and the submaxillary glands, purulent parotitis, abscesses in the ear, premature birth in a woman who died five days later of insanity, convulsions in women during menstruation, an exanthem resembling scarlet fever, an eruption on the lips (herpes labialis?).

It may be mentioned finally that Gluge also speaks of an extension of this epidemic in America and China, giving as his authority A. Fothergill. Webster is silent on this subject. According to Ozanam the influenza is said to have prevailed also in this year on the Island of Bourbon.

Epidemic of 1780–81.

This epidemic began in January, 1780, in France; in March it had extended to Lothringen and to Heidelberg, and at the same time it appeared in Italy.

Sigaud informs us that in March of 1780 the influenza also appeared in Brazil (Rio de Janeiro), where the disease received the name of "zamparina." In September, 1780, influenza appeared again on the southern coast of China; during the winter months it prevailed

in Russia (St. Petersburg, Willna), and in the spring of 1781 we find it in America.

We possess only meagre accounts of this epidemic. Gilibert mentions the extraordinary morbidity of the disease in Russia. The symptoms of the influenza in America are given by Webster as: severe pain in the head (twenty-four hours), prostration of strength, coldness and chills, pain in the side resembling a rheumatic pain, troublesome cough, and difficult respiration. As regards the mortality he states that the disease was not dangerous, but that its effects were seen the following year in the increased number of cases of phthisis.

Speaking of this epidemic we find in the "Medical Transactions" (London, 1785) an account of the outbreak of the influenza among the crew of a vessel on the high seas. It occurred on the *Atlas*, which was bound to Canton from Malucca.

Epidemic of 1781–82.

This was one of the most widespread pandemics of this disease that have ever occurred, and consequently the literature on it is very extensive.

According to Hirsch, who furnishes us altogether with forty-three authorities on the epidemic of this year, the disease made its first appearance, in the autumn of 1781, in China and India, and then passed through Siberia or Russia and invaded St. Petersburg in January, 1782. From St. Petersburg the pestilence travelled over Finland, Esthland, Kurland (Riga), along the coast of the North Sea to Germany. From March to August the influenza then spread over Germany and nearly all the other countries of Europe. It visited Denmark (Copenhagen) and Sweden in April. In England, Newcastle-on-Tyne was first attacked (towards the end of April, 1782); in May it had reached Norwich, St. Edmunds, and other cities to the south. In London, and at the same time in the cities lying west and southwest, Bristol, Bath, Oxford, Plymouth, it raged during the second half of May. It then invaded Scotland (Edinburgh).

In Germany, the influenza occurred in the northern, middle, and southern parts, in April and May. In the month of June, the epidemic travelled to the Netherlands, from there to France in the first half of June, then to Italy, and lastly, in August, to Spain.

For a better understanding, the course of the epidemic is here shown in a table in which the towns are placed under the months in which they were invaded.

Autumn, 1781.	January, 1782.	February, 1782.	March, 1782.	April, 1782.
China. India. Spring. America.	Moscow. St. Petersburg.	Reval, Riga. Tilsit.	Germany: Memel. Königsberg. Dantzig. Strahlsund. Greifswald.	Copenhagen. Germany: Berlin. Magdeburg (Lippe). Hassbrooken, Jena. Göttingen. England: Newcastle-on-Tyne.

May, 1782.	June, 1782.	July, 1782.	August, 1782.
Germany: Prague. Hamburg. Dresden. Frankfort. Vienna. Munich. England: Norwich. Portsmouth. Greenwich. Guilford. London. Bristol. Oxford. Scotland: Edinburgh.	Germany (south). Netherlands: Brussels. Amsterdam. England. Scotland: Glasgow. Ireland: Dublin. France: Bordeaux. Brittany. Paris. Italy: Ancona. Spoleto. Rome. Florence. Parma. Venice.	France: Orleans. La Rochelle.	Spain: Madrid.

The views concerning the origin of the epidemic are variable. Gluge believes that the epidemic already existed in September, 1780, as also does Schweich.[46]

According to English writers,[48] the epidemic of 1782 is believed to have had some connection with the occurrence of influenza in India in November, 1781, the English army having suffered severely during the siege of Negapetam. Wittwer,[49] Languth, and others begin the history of its dissemination with the appearance of the disease in St. Petersburg, in the month of January, 1782.

An exact historian of 1782 is Metzger,[50] who collected the reports of eleven physicians in Prussia on the epidemic. He says that the influenza, Russian catarrh as it is named by him, was so universal in March that in very many houses all the inmates were attacked.

Brush mentions as a symptom the danger of suffocation, with cough, and as complications, swelling of the glands of the neck, called swelling of the parotids by Mehlhorn. Tiefenbach mentions hemilateral cephalalgia accompanied by ocular inflammation and delirium, also an exanthem of the hands and feet as a complication during recovery.

The following complications are also mentioned, besides phthisis, pneumonia, pleuritis, etc.: Dysuria, which passed away with the dis-

ease, abortions and disturbances of menstruation, and suppuration of the ears.

As a general rule, the nervous symptoms were reported to have been especially prominent in this epidemic. Some authors designate the epidemic as a "bilious" one, and Schweich also describes as most frequent symptoms, "inflammation of the liver, yellow jaundice, bilious stools and urine, and bilious vomiting."

When we read that in St. Petersburg thirty thousand, in Königsburg one thousand persons daily were stricken with the disease, that also in Rome two-thirds, in Munich three-fourths of the inhabitants were attacked, that they were compelled in Vienna to close the theatres for eight days, we are convinced without further argument of the great morbidity of this epidemic. Children were not attacked so frequently in proportion as adults.

In this epidemic, the observation was made that the influenza, which in itself was not dangerous, still had a marked tendency to raise the death-rate of some cities, as, for example, in London and Paris. Thus we read in the Medical Transactions,[48] that in London, in a single week, from the 5th to the 11th of June inclusive, 560 deaths occurred altogether, and out of these 560, 121 were marked as having resulted from "fever."

The extraordinary reports of the etiology of the disease are interesting. The Consilium Medicum at Vienna referred the cause of the epidemic to small insects, which had been swallowed. The famous philosopher Kant also believed that the air had been vitiated by noxious insects brought in from China. Haygarth (Thompson's "Annals" [1]) opposed the idea that the influenza was disseminated by the wind, arguing that, if that were the case, the disease would have to travel through Great Britain in twenty-seven hours. Schönlein, observing that the influenza had taken four days to travel from Königsberg to Berlin, compares the rapidity of its march with that of a horse. Crell incriminated the increased volume of electricity in the air. Mertens did not believe the influenza a contagion, for the reason that, according to his observation, now only one, and then again all of the members of a family were stricken.

It may also be remarked that Gallicio[51] observed in Venice that the stubborn tertian fever which had afflicted the people for a long time ceased with the advent of the influenza.

The Medical Transactions[48] furnish us with a few more examples of the occurrence of the influenza on vessels: On the ship *Goliah*, which sailed from Spithead, the influenza broke out on the 29th of May on the high seas, no contact with land having been made during this time. The ships *Rippon* and *Princess Amalia* belonging to a

large English fleet, which sailed on the 6th of May from England, were attacked by the influenza on the high seas towards the end of May.

Epidemic of 1788–89.

This prevailed, like the preceding, throughout Europe, but was not so fully described, which may have been, as Gluge[16] says, for the reason that "the physicians seem to have exhausted themselves in the description of the previous epidemic." We are informed that the epidemic travelled successively through Russia, Germany, Hungary, Denmark, England, Scotland, France, Italy, and Switzerland, from March to October of this year.

In this epidemic Simmons[52] describes the occurrence in all patients, besides the usual symptoms of influenza, of pain in the scrobiculus cordis, which extended in some along the whole line of the sternum. Patients who complained of neither cough, vomiting, nor diarrhœa, nevertheless suffered from this symptom.

Grill[53] gives a very good description of the symptoms of this disease, among them being "a general debility, extraordinary hebetude, a heavy head, a heaviness and numbness of the lower extremities, weakness and confusion of the senses, dull eyes, a sensation of pressure in the region of the stomach, tightness over the chest, and difficult respiration."

Zeviani mentions as complications of the "mal di mazucco" swelling of the testicles, pain in the ears, pain in the eyes, toothache, etc.

In the year 1789 influenza prevailed widely in America. We are not justified by the existing records in regarding this epidemic as a direct continuation of that existing in Europe in 1788, although its probability may be suspected. For nearly one year nothing is heard of the influenza, as it had died out in Europe in October, 1788, and did not make its appearance in America until the autumn of 1789. Webster[1] says that it made its appearance first towards the end of September, 1789, in New York and Philadelphia, and it is said to have been imported into Philadelphia by the members of Congress returning from New York, about October 1st (Rush[42]). The disease then extended rapidly over the whole country. It reached the West Indies (Jamaica) in October, at the same time that it was ravaging the New England States. In November it invaded Massachusetts; in December Nova Scotia, having already manifested itself in South America. The epidemic ran an extraordinarily rapid course. Webster says: "It appeared in the West Indies nearly at the time it did in the Northern States; it overspread America from the 15th to

the 45th degree of latitude in about six or eight weeks." The native Indians were attacked as well as the whites.

As a proof that the influenza was not spread by "infection," Webster adduces the fact that sailors one hundred miles from land, "who as to infection were entirely insulated," were also attacked.

A recurrence of the disease in the spring of 1790 in North America, namely, in Albany, Boston, New York, and elsewhere, is reported by Hirsch.[8]

Epidemic of 1799–1800.

This was an unimportant epidemic, confined to northeastern Europe, which spread during the winter and the following spring from Russia to Galicia, Poland, Germany, and Denmark.

In the nineteenth century we meet with the records of influenza epidemics in literature much more frequently than previously. One reason for this is that commerce between nations had become more frequent, and that the records of epidemics among those who were interested could be better exchanged; for it is undoubtedly true that many an epidemic of former centuries has been lost to literature simply because the external circumstances for the dissemination and recording of news were unfavorable.

If we look over the table of A. Hirsch[8] we find that there have been comparatively few years in this century in which we have not an account from somewhere of the influenza, be it as local epidemics, or as widespread epidemics or even pandemics.

A very detailed history of influenza of our century would take us too far, and we can study, therefore, only the most important epidemics.

As pandemics of influenza during the nineteenth century, there are generally recognized those of 1802–1803, 1830–1833, 1836–37, and 1847–48; while Hirsch also adds those of 1850–51, 1855, 1857–58, and 1874–75, leaving out, of course, the latest influenza epidemic, which, as we know, began in the year 1889.

Epidemic of 1802–1803.

This made its appearance during the winter of 1802 in France, although the disease had prevailed during the last three months of the year 1800, and in the beginning of the year 1801, in Germany and France, as well as in China[9] and Brazil (Rio de Janeiro). It spread during the months of January, February, March, and April of the year 1803 over Germany, Italy, England, and Switzerland (Central Europe).

The mortality in this epidemic was small, only the abuse of venesection brought many to the grave. Thus, so many farmers are said to have died in Russia from it that venesection was forbidden by an imperial ukase. Jonas says that many patients were bled either on the advice of a simple village barber or by their own wish, and most of them died. In Prussia also bleeding was declared detrimental by the Government.

Nearly all authors agree that this epidemic involved the nervous system to a great extent, great depression, as in typhoid fever being present, and the patients had to undergo a long period of convalescence. This was especially noticed in England, and was described by English authors, who again emphasized the great danger to which this disease exposed old people and phthisical subjects. In France (Paris) there were observed, according to Schweich, coryza, tonsillitis, pleuritis, bronchial catarrh, suffocation (asthma), and intestinal catarrh, as the usual and most common symptoms, whose general character inclined occasionally more to that of inflammatory affections, and again to septicæmia.

Concerning the spread of influenza between the years 1805 and 1830 the following may be briefly mentioned. After the influenza had appeared generally in the West Indies and in Spain, during the winter of 1805 to 1806, it made its appearance again in Russia in September, 1806, showed itself in November, 1806, in Germany and France, and in Italy in January.

In the year 1807 the influenza was generally disseminated throughout North America. It broke out in Massachusetts in February, in the other New England States in the spring, and in the western part of America in the autumn. In November and December of 1807 it prevailed in Scotland and England, being still present in Newcastle in January, 1808. According to Sigaud, the influenza next appeared in Brazil in the year 1811.

In the autumn of 1815 we find it again in North America, appearing in Boston in September of this year, in the following month in New York, during the winter in Pennsylvania. In February, 1816, it visited the State of South Carolina, and was present at the same time in Brazil.

During the years 1824, 1825, and 1826 influenza again visited the United States; it was present in Boston in October, in the following month in New York, in September in Philadelphia. In January, 1828, it showed itself in Georgia and Alabama, in February on the Atlantic seaboard as well as in the eastern, northern, and western parts of the United States. In May it was present in Mexico, in September in South America (Peru). In 1827 the influenza was also

epidemic in Siberia and Russia during the months of January and February, without, however, spreading to the rest of Europe.

Epidemic of 1830–32.

According to Bennet, the influenza prevailed in China in January, 1830, as also in the month of September of this year in the Philippine Islands, and especially in the city of Manila, from which place, according to most historians, this epidemic is said to have taken its start.

Two months later, namely, in November, 1830, the occurrence of the influenza was reported in Moscow; in January, 1831, it arrived at St. Petersburg, and at the same time it prevailed on the islands of Borneo and Sumatra; Java was visited by it in March. In the mean time the influenza found its way from Russia through the Russian Baltic provinces, and entered Germany by way of Poland (Warsaw); it appeared in eastern Prussia and Silesia in April, 1831, spreading in May and the two following months over the whole of Germany. In June and July it prevailed in France, England, Scotland, Sweden, Belgium, and Switzerland, reaching Italy in November. In December, 1831, we find the disease present in Naples and in Sicily; in January, 1832, it appeared in Spain (Gibraltar). With this, the epidemic terminated its career in Europe.

In February, 1832, we hear of the disease in America, in the State of Georgia, after it had already invaded New Jersey three months previously in November, 1831, and made its second appearance in Philadelphia in January.

If we take Manila as its place of origin, this epidemic travelled in general from east to west. For it broke out in Manila in September, reached Russia in November, Germany in April, and Belgium and France in June; it then branched off to the right and left (Denmark, England, and Italy, similar to its march previously from Manila to Borneo, Sumatra, etc.), and in January it had reached as far as Gibraltar, in Spain. Three months earlier, in November, 1831, it was already present in North America, prevailing in Georgia in the month of February, 1832, and again reached Asia (upper India) in the same year. Thus, the epidemic finished its course around the earth, in this march from east to west, from September, 1830 (Manila), to April, 1832 (upper India), in about two and a half years.

The influenza took exceptionally long to travel from Manila (September, 1831) to the neighboring islands of Borneo and Sumatra (January of the following year), while it reached Moscow in November, 1831.

Except for this we do not find anything very interesting recorded about this epidemic. Its morbidity was again enormous. The disease, according to Kahlert, made no distinction between age, sex, or rank, but, according to Leberecht, persons of middle age, especially women in the climacteric period, were attacked with especial frequency, and, according to Krimer, children under fourteen years of age and adults over forty-five years were spared by the influenza. In Paris, where it remained nearly an entire year, the number of deaths in that period is said not to have been larger than usual.

Heidenreich [36] distinguished four varieties, the catarrhal, nervous, gastric, and inflammatory forms.

Epidemic of 1833.

This was another pestilential march through upper Asia, Europe, and North Africa. America, so far as we know, escaped; so it seems that this epidemic was confined to the Eastern Hemisphere. Nevertheless, the literature on this epidemic is much more voluminous than that of the previous one of the years 1830–32, for which Hirsch mentions some fifty authorities, while the number of authorities cited by Hirsch for the epidemic of 1833 reaches the figure of one hundred. It is most probable that the epidemic of 1833 also had its origin in Asia, for we know that the influenza reigned in upper India in December, 1832, and a few weeks later, in January, 1833, we already meet with it in Russia, as, for example, in Moscow, St. Petersburg, and Riga.

Just as in the beginning of the year 1831 (the last epidemic also attacked St. Petersburg in January, there had passed therefore for St. Petersburg since then exactly two years), the influenza now begins its march from Russia, through Europe, etc.

The disease reached Memel, in Prussia, near the frontier, in February, spreading in March (Berlin) and in the following months over the whole of Europe. At the same time it made a wide detour to the south and southeast, invading Odessa on the Black Sea in February, Brody, in Galicia, in the same month; in March it prevailed in Constantinople, and travelled in this month as far as Syria and Egypt. The northern countries, Denmark and Sweden, were invaded in March and April. In April influenza also visited Hungary (Pesth), France (Paris), and Great Britain (London, Edinburgh). In Italy it made its appearance first in May, in June it invaded the Netherlands, in September Switzerland, and by November it had passed through the whole of Italy as far as Sicily, where this epidemic terminated.

All the historians agree as to the unexampled morbidity observed in this epidemic. In St. Petersburg, "not one person escaped the influenza" (Lichtenstaedt). In Prague, "scarcely a house was spared by the plague" (Kahler). Hufeland mentions that in St. Petersburg 10,000, in Memel 8,000 out of 10,000, in Berlin at least 50,000 inhabitants were attacked. The *Gazette Médicale* gives the figure of morbidity as four-fifths of the whole number of inhabitants of Paris. In Königsberg, according to Hufeland, parents, children, and servants were frequently smitten with the disease at the same time, so that strange help had to be obtained for the family. Metzger had made a similar observation concerning the epidemic of 1782.

A marked increase of mortality was noted in Königsberg, where one hundred and five persons died during the last week of March, while only about forty to fifty deaths usually occurred in this month.

According to Kahler, the sequelæ of influenza caused many deaths in Prague, and Rafanovic estimates the mortality during the epidemic of 1830–33 to have been about one-seventh of all that were taken ill (cited by Hermann). On the whole, however, the mortality was not much increased by the influenza in this year, and in Bohemia, it is said, the mortality was even less than usual. One fact should, furthermore, be mentioned, namely, the observation was made that other diseases during the influenza epidemic diminished in frequency and violence; this was true in Austria and Bohemia, as well as in Königsberg.

Concerning the etiology, it may be mentioned that Hufeland [66] believed it to be due to air-infection, and Zlatorovich [67] attributed it to telluric influences, and was, furthermore, of the opinion that the epidemic became more violent when the moon was nearest the earth. In concluding the account of this epidemic, we may also mention that in the following year, that is, 1834, influenza raged in Cayenne in January, in Calcutta in February, and in Brazil (Rio de Janeiro) in December.

Epidemic of 1836–37.

This again ravaged particularly the Eastern Hemisphere. It appeared in Europe first in Russia (St. Petersburg) in December, 1836. One month previously it had already visited lower India and the Island of Java, contemporaneously prevailing in the southern point of Africa (Capetown). In Sydney, Australia, the disease is said to have been present in October. The question as to the starting-point of the epidemic seems to be rather obscure, unless we refer its

origin, analogous to that of the preceding epidemics, to Asia, namely, in India and Java in November, 1836.

Nearly at the same time that it appeared in St. Petersburg, the scourge invaded Sweden, Denmark, Germany (Berlin), and England. In January, 1837, it again visited Egypt and Syria, as also France, Ireland, the Netherlands, and Switzerland. In February, 1837, the disease reached upper Italy, also Spain and Portugal; in March it was still present in some parts of Southern Europe and in Switzerland; in July it appeared in the Faroë Islands. According to Hirsch, the influenza prevailed also in Mexico in March, 1837; the morbidity was again very high. One of the historians, who had personal experience of this epidemic, was Gluge. He says, among other things, that two-thirds of the scholars were absent from the Gymnasia in Paris; that among 1,200 patients who reported to the Central Bureau in Paris, there were 1,050 suffering from influenza, and in Berlin about 40,000 patients suffered from the disease. The epidemic was also very prevalent in Milan, Siena, Rome, Bologna, and Pisa (Pétrequin[65]). In Vienna only very few persons escaped entirely in 1837 (Sterz). The influenza also prevailed throughout the whole Prussian army.

Most of the patients were adults from twenty to forty years of age, and of these more women than men were attacked. Curiously, however, the physicians of Würtemberg speak of the great dissemination of the disease among children.

In Paris and London the mortality was considerably increased by the influenza of this year. Hermann even asserts that in Dublin about forty thousand persons (?) fell victims of the disease.

In London there died, during the week ending January 24th, 1837, a total of 871 persons, and among these deaths there were 295 from diseases of the respiratory organs; during the week ending January 31st, out of a total of 860 deaths, there were 309 from diseases of the respiratory organs.

The complication most frequently present in this epidemic was pneumonia. French authors were the first who had their attention drawn to the peculiarity of the pneumonia of influenza and pointed it out. According to Piorry[66] the latter differs from ordinary pneumonia, in the first place, by its complicating a bronchitis, by its gradual development, and by the peculiar physical signs in the lungs; the respiratory murmur is at first diminished, later it becomes absent altogether, then bronchial breathing appears, without the recognition of dulness or crepitant râles, as we find in true pneumonia. According to Nonat,[67] the pneumonia of influenza rarely makes its appearance before the second or third day of the influenza; occasionally even after

five to six days, Nonat himself could frequently demonstrate only rhonchi and rattling sounds over the whole lung. Out of sixteen patients eight died. According to Vigla[41] influenza aggravated chronic diseases of the respiratory tract, especially tuberculosis of the lungs; it also had a bad influence on the nervous system, especially the spinal cord.

The following other complications or sequelæ were observed: Psychoses, for example, mania, neuralgia, apoplexy, paresis, paralysis, swelling of the parotid gland, meningitis, abscess of the ear, uterine hemorrhage and abortion, miliaria and urticaria. As regards the general symptom complex, we may quote the words of Pétrequin as follows: "In all cases there was observed by the physicians a functional disturbance of the nerve centres previous to the local symptoms. No matter how diverse the other symptoms of the disease may have been, one organ always seemed to be attacked, namely, the brain and spinal cord; to this there were added, as the most frequent complication, the disturbances of the chest and abdominal organs."

In regard to the occurrence of influenza during the years 1838 to 1847, the following brief résumé must suffice. Nearly every year of this period furnished its epidemic of influenza, the year 1840 alone excepted:

The disease prevailed, according to Hirsch:

In 1838—in February, on the Island of Bourbon and in Iceland; in November, in Australia (Sydney) and New Zealand.

In 1839—in Abyssinia.

In 1841—in January and February, in Germany; in March, in Germany and also in Hungary (Pesth); in April, in Germany, Hungary, and Ireland (Dublin).

In 1842—in January, in Belgium; in March, in England (London); in the spring, in France (Paris), also in Egypt and Chili.

In 1843—in March, in Germany, England, and Iceland; in April, in France (Paris); in May, in Northern Siberia; in the summer, in North America greatly disseminated, during June in the New England States, New York, and the West; during July in Pennsylvania, the Middle and Southern States, Virginia; and during August, in South Carolina.

In 1844—in January, in Germany and England; in February, in France and Switzerland; in November, in Cayenne.

In 1845—in January, in Germany and in Switzerland.

In 1846-47—in winter, in England, Denmark, Belgium, Switzerland, and France (Paris); in February, in Russia; and March and August in Turkey (Constantinople).

According to Doellinger," the influenza also prevailed in Brazil (Rio de Janeiro) in the winter of 1846-47, where the name of "polka fever" was given to it.

Epidemic of 1847–48.

With the exception of St. Croix, St. Vincent, and a few other West India islands, the Eastern Hemisphere was the chief sufferer in this epidemic. As mentioned above, the disease prevailed in Constantinople in August, 1847. In September and October it visited the south of France. Soon after it appeared in Germany, where it became general in November, December, and January; at the same time it was disseminated in the other countries of Europe: the Netherlands, Denmark, and Great Britain. In December the influenza travelled to Switzerland, to upper Italy and the Riviera, to Spain (Madrid), as also to Greece, Egypt, and Algiers. In the same month it visited the north of France (Paris) and Scotland. In January we find the disease present in lower Italy and the south of Germany. This epidemic, like the previous ones, showed a high morbidity. According to Marc d'Espine," there were attacked by the influenza: in Paris, one-fourth to one-half; in Geneva, one-third of the whole population; in London, about two hundred and fifty thousand persons are said to have been seized with it.

Among the adult influenza patients, there are said to have been more women than men; according to Canstatt, there were proportionately more children than adults attacked.

One fact is dwelt on strongly in this epidemic, namely, the increased mortality. Peacock says that the mortality was raised in children 83 per cent.; in persons from fifteen to sixty years of age, 104 per cent.; in persons over sixty years of age, 247 per cent.

Lombard's report of the desolation caused by the disease in Belgium characterizes influenza as a disease which should not be lightly spoken of.

Epidemics from 1850 to 1889.

In the beginning we may mention that the influenza made its appearance very frequently during this period, at some point nearly every year, covering larger or smaller territories. During this time there occurred some quite extensive epidemic invasions in 1850-51, 1855, 1857–58, and 1873–75, but they do not compare, as regards extent and intensity, with the already mentioned pandemics of our century—1831, 1833, 1837-38, and 1847-48.

In the winter of 1850–51, the influenza prevailed throughout the

whole of America; in December it occurred first in Martinique, and then travelled over the western coast of South America, from Peru to the lower part of Chili.

In January it visited North America (California), beginning in this month also in Europe, where it first invaded Germany and Sweden in February, and in March, France (Paris) and Italy, as well as the north of Africa (Egypt).

In the year 1852 we find influenza present in Australia and in Tasmania, as well as in the South American states of Peru and Chili as in the previous year.

Influenza was present in May, 1853, in the Faroë Islands. One year later it prevailed in some districts of Bavaria.

In the year 1855 Europe especially was invaded by the influenza, and that with an enormous rapidity, for in January this disease prevailed in St. Petersburg, and had reached, by way of Germany in the same month, both the Netherlands and Italy, including even Naples, which, as a rule, was visited much later.

According to Doellinger," the disease also prevailed in Brazil (Rio de Janeiro) in June of the same year, curiously though only among the whites, while the blacks were not at all, and the mixed races only very rarely affected.

In the epidemic of the year 1857–58, both hemispheres were again the sufferers, the Western as well as the Eastern, which led Seifert to call it "one of the greatest of epidemics." The disease occurred first in America, in August in Panama, in September in the West Indies and along the western coast of South America (Chili and Peru), as well as in British America (Vancouver's Island). In the Eastern Hemisphere it was confined to Europe. In December, it prevailed there successively in Russia, Germany, Belgium, and France; in January, it had reached Italy (Naples); in the middle of February, Greece (Athens). The epidemic was attended by a very high rate of mortality in Rome and Naples; in Rome it is said to have been even higher than at the time of the cholera. In Strasbourg also the mortality is said by Wolff to have been excessive.

As regards the nature of influenza, the views of Hagen, founded upon a study of this epidemic, which are also indorsed by several recent authors, may be briefly mentioned. He believes influenza to be miasmatic-contagious, the contagion being developed by the patient himself. A certain amount of this, which accumulates in the air, may then cause an epidemic in different localities; it cannot, however, be transferred from one patient to another.

In the following ten years (1860–70) influenza made its appearance very irregularly. In June and July, 1860, it appeared on the conti-

nent of Australia, as also in Tasmania. In December of the following year it presented itself in North America (Philadelphia). In the year 1862 it prevailed in January in the Bermuda Islands, as also in the Netherlands (Rotterdam).

In the winter of 1863–64 an epidemic of influenza appeared in New Caledonia and also in California, then in France (Paris) and Switzerland, in May also in Africa.

In the year 1866 influenza prevailed in Paris, in May in London, in December it appeared on the islands of Réunion and Mauritius.

France (Paris), Germany (Stuttgart), Belgium (Ghent) were again invaded in February, March, and April of 1867; in the following year the disease, so far as is known, appeared only in Turkey.

In January, 1870, influenza again presented itself in Russia. It also visited Denmark, Sweden, and individual cities in Germany in the same year.

In 1870 the disease was present in Norway, and then it did not appear epidemically again until 1873 when it prevailed from January to March. During the winter of 1874–75 it occurred extensively in America, and it also spread in this winter to Germany, France, and Sweden. In 1873 it prevailed in the United States, being generally disseminated through Pennsylvania, Ohio, Virginia, Illinois, Iowa, Michigan, Wisconsin, Minnesota, Missouri, Alabama, Louisiana, and Texas, and in the winter of 1874–75 nearly all these States were attacked for the second time.

In the spring of 1879 influenza again visited America. In St. Petersburg it showed itself anew each year, from 1885–88. In the spring of 1889 it visited Greenland and the Hudson Bay territory, and in the month of May of this year again invaded Russia, especially Bokhara. From here we find the great influenza epidemic of 1889–90 take its origin, exceeding by far any previous invasion of the disease.

Epidemic of 1889–90.

As, after a short lull the storm rages anew over the land, so this influenza epidemic broke forth from the East, and overwhelmed the world in a pandemic such as had never before been seen.

The high flood of the pandemic flowed over the whole globe in the space of a few months. When we consider the manner of its dissemination, its rapid progress causes great astonishment, although we are accustomed to view all possible remarkable phenomena in nature. This flood, however, was followed by many small currents, which slowly disappeared; in 1893–94 another influenza epidemic appeared in many places, and was rightly looked upon as a recrudescence of

the former epidemic. Intermediate between these two epidemics of 1889–90 and 1893–94 there has not been any period of time altogether free from the influenza. Here and there individual cases, or small endemics, have been separately observed.

In the first half of the year 1893 a light spring epidemic appeared, and in November, 1893, a larger epidemic began to spread over Europe.

A sudden increase of deaths and acute diseases of the respiratory organs corresponds to this outbreak. In the third week of November, for example, there were observed: in Hamburg 202, in Frankfurt about 106, in the district of Düsseldorf 27; in the fourth week of November, respectively 818, 248, 163 cases of influenza. The remarkable increase of deaths was first observed in a few cities of Central and Western Europe, later also in the northern part. Although it existed at the same time in the surrounding countries, an importation from either side cannot be proven with certainty. Rahts leans to the view that a simultaneous outbreak had occurred at different parts.

The height of the epidemic was rapidly reached, for the most part, in December. In individual cities, among them Munich, Augsburg, Breslau, and Dresden, the mortality figures rose for the second time towards the end of the epidemic. The extinction of this epidemic took place in March, 1894. As a rule, the inhabitants of the country seem to have suffered more than those of cities. No age was spared, but persons between twenty and fifty years of age were attacked by preference. No trade was a sure protection. It is mentioned that the postal, telegraph, and railway employees, and particularly the travelling personel of the latter, were chiefly attacked.

The great pandemic of 1889–90 gave many occasions for observations which are of the greatest importance for the recognition of the epidemiology of influenza. For the greatest part, this is based on the fact that the epidemic gave an incentive to scientific discussion with a special impulse to collective study, and thereby to a proper estimation of individual observation. It is necessary, therefore, to the scientific treatment of the influenza question, that this epidemic be carefully studied.

In the last quarter of the year 1889 influenza appeared epidemically, first in the eastern portions of Europe, then in the central and western portions. During the first months of the year 1890 it spread farther and farther, travelling through all the countries of Europe, extending to America, Africa, and Australia, so that we may truthfully designate its appearance in 1889–90 as "pandemic."

We are able to trace its origin in Central Asia. In the second

half of May, 1889, it appeared in Bokhara, dying out there only in August of the same year; it then travelled to Siberia, where (at Tomsk) cases of influenza were observed with certainty in October, having already previously invaded the Caucasus and European Russia.

In St. Petersburg it spread over the whole city, in October, 1889, dying out only in December, in the mean while extending to other cities of Russia, also to Abo, Stockholm, Copenhagen, Paris, Berlin, Vienna, Brussels, and London. It appeared in Asia Minor early in January, 1890, and also in Rome, Constantinople, and Athens. Towards the end of 1889, and in the beginning of 1890, it prevailed in Fez and Tunis, later in Mexico, South America, and Australia, thus sparing no climate and showing itself in hot as well as in cold seasons, in the plains as well as at elevated points. In all places the chief commercial cities were first attacked; and thence the plague spread to other localities, and lastly, invaded the country districts.

The contagious properties of influenza, which were at first doubted by many, were very soon established. It was only a question whether the patient alone carried the infection, or whether the latter was disseminated by the clothing of healthy persons who had come in contact with patients suffering from the disease. People of all ages were attacked, those in all conditions of life, and individuals in every trade. The course of the disease in general was favorable and also quite rapid; unfavorable only in many children during the first few years of life, in many old people, in many debilitated persons, and especially in those suffering from chest affections.

While it is certain that the first cases of the disease occurred in the East, and that the plague travelled by way of Asia to Russia and the rest of Europe it nevertheless seems that, after it had reached busy Europe the avenues of trade now influenced its dissemination in a greater degree, as to its direction and rapidity, than the inclination formerly ascribed to it of travelling from East to West. Its appearance as Siberian fever in the district of Viatka in Eastern Russia, in October 13th, and in Tomsk (Siberia) about October 28th, has been verified.

Between the middle and end of October the first cases of the disease appeared in St. Petersburg, and in the beginning of November in Moscow, Wilna, Riga, and Sebastopol. In rapidly following succession the surroundings of St. Petersburg were invaded by the epidemic, and in the latter days of November there could be no more doubt about the outbreak of the disease in Berlin.

In Germany, Berlin and Charlottenburg were the first cities to

be attacked by the disease, preceding, however, by only a few days the cities on the shores of the Baltic; Danzig and Kiel were next attacked, then Altona and Potsdam and the large commercial cities, Halle, Leipsic, Dresden, Frankfort-on-the-Main, Essen, and Dortmund. By this time such a number of large foci were formed that it was impossible to say whence arose the new sources of contagion.

Although the disease in Germany invaded so many localities in a short time that the individual foci could not be distinguished from each other, we may yet gather an idea of the velocity of the dissemination from the following statistics. The first appearance of the influenza in 998 localities distributed over the whole of Germany (cities and villages) was recorded as follows: End of October, in 150 localities; beginning of November, 12; middle of November, 16; end of November, 62; beginning of December, 103; middle of December, 450; end of December, 307; beginning of January, 33.

The work on the epidemic of grippe in the German army, 1889–90, designates the ports of the Baltic as the door of entrance of the plague for the German garrisons, and shows that the influenza spread very rapidly (in five weeks) from northeast to southwest, to the most distant points. The total number of persons affected in the army and navy was 55,263, or 10.5 per cent. to the Sixteenth Army Corps, 20 per cent. of the two Bavarian corps; the mortality was 0.1 per cent.

A determining factor of the dissemination of the epidemic was not the weather, but human intercourse, and especially commerce. We all remember the "explosive" appearance of the epidemic in numerous localities at the same time, which led to many false beliefs. It was believed that there could hardly be found a scale to measure the velocity of its progress. Thus Collin remarked before the Paris Academy in the year 1889: "The grippe is independent of any kind of human intercourse. It travels through densely populated localities and uninhabited regions with the same velocity as light and air." It is not to be marvelled at, that the newspapers of that period also published the most wonderful flights of imagination, that the germs of the disease were aëriform, or that they filled great spaces in high regions like cosmic dust to be precipitated from thence on to various portions of the earth's surface at the same time. At present, we know that the pandemic is not more quickly disseminated than would be possible by our most rapid means of travel, the railroads and the ocean steamers. At the same time, however, we learn that the pandemic of 1889–90 travelled far more rapidly than that of 1830–31; another proof of the fact that its dissemination is linked to com-

merce. A very good presentation of this has been given by Leichtenstern in the following table:

Month.	1889-91.	1889-90.
First.....	Moscow.....	St. Petersburg, Moscow, Curland, Livland, Finnland.
Second....	Russia	Berlin, Paris, Vienna, Sweden, Denmark.
Third.....	St. Petersburg	London, Holland, Belgium, Balkan states, North America.
Fourth....	Curland and Livland.....	Capetown, Egypt, Honolulu, Mexico, Japan, Hong-Kong.
Fifth.....	Warsaw	San Francisco, Buenos Ayres, India, Sierra Leone, Sicily.
Sixth	Eastern Prussia and Silesia ...	Chili, Kamerun, Zanzibar, Basutoland, Tasmania.
Seventh...	The whole of Germany, Finnland, Denmark, Vienna.	British Bechuanaland, Barbadoes.
Eighth.. .	Paris, Belgium, Sweden, England, Scotland.	Gold Coast, Natal.
Ninth	Switzerland.....	Trinidad.
Tenth.....	Italy	Iceland, Madagascar, China, Senegal.
Eleventh..	Spain, North America.....	Cashmere, Katun Alps.

The dependence of the spread of the epidemic on commerce is made very evident by the fact that the disease frequently spread more rapidly from a trading centre to capitals and other commercial cities, than from the latter to the villages in their vicinity. Thus, it happened frequently that the railroad towns were earlier attacked, while places having but little commerce, for example, towns on the Russian-German frontier, numerous country districts, as in Thuringia, and the Black Forest and the Bavarian Forest, were visited only at a late period by the scourge. In localities sparsely settled, and in widely separated villages, the influenza frequently spent more time in spreading through a small territory than it needed for its dissemination to all the chief cities of Europe and even to cross the ocean. In some of the country districts in England the influenza consumed four months (December to March) in its invasion; while in industrial districts a few weeks only were needed for the same purpose.

We, however, meet also here with remarkable differences, as is the case in all epidemics. Influenza being preëminently a disease of the respiratory organs, it is easy to understand that external factors, such as the weather, etc., will favor or retard its dissemination. This is especially brought to our notice when we read of the exceptions to the general rule of the rapidity of dissemination of the disease. Thus it is said, for example, that in the district of Bradwell, which has little commerce and consists of widely separated farm-

houses, a very rapid dissemination took place, whereas elsewhere in England its progress was remarkably slow. After London had been infected on December 11th, the cities of Birmingham, Manchester, Glasgow, Sheffield, Liverpool, and Edinburgh were not invaded until the end of December or the beginning of January.

There are a few localities which entirely escaped a visitation. These were the Isle of Man, the West Indies, the Bahamas, Grenada, St. Lucia, British Honduras, British New Guinea, and the Seychelles. The influence of commerce was well shown in a few instances, in which influenza occurred only late, because up to that time there had been an entire interruption of commercial intercourse. The island of Borkum had no intercourse with the mainland from Christmas to January 5th on account of the intense cold. On this date the first passenger boat arrived, and four days later the disease broke out. Vladivostok and the Island of Saghalien were only invaded in the spring of 1890, after communication by boat had again been opened. In some villages on the Weser, which had been cut off from all communication for weeks by a flood, the disease did not make its appearance until communication was opened again. The spread of influenza by bounds and leaps is also probably due to the irregularity of intercourse. Thus, it is certainly curious that Paris and London were earlier visited by the plague coming from Russia than many cities of Germany. In Boston and some other North American cities the disease appeared earlier, or at least as early as in England. It seems to have visited Boston before New York. For this reason some authors point out that North America was probably infected by way of Siberia, from the west therefore. This probability is also borne out by the fact that cases of the disease had already occurred on a steamer which was under way from Japan to San Francisco, in the beginning of December. Remarkable as these leaps are, they do not prove that there is no law of dissemination, and are not inexplicable.

Places lying along large commercial routes were always first attacked, and after them the parts having little business. We must not forget here that the localities having constant intercourse with the outside world in all probability reported the first cases of the disease with greater promptness. It is also likely that the first cases occurring in such places where a physician was near at hand were more easily recognized.

All the facts point in the direction that commerce exerts an important influence in the dissemination of this disease, but the question remains whether other influences are also at work.

Local Epidemics.

In reviewing the literature of former periods and in our modern observations, we frequently meet with reports of strictly local epidemics of influenza, confined to one city, to circumscribed portions of a city, or even to certain houses in one or several different districts. This is naturally of great interest from many points of view, and we are confronted at once with the important question whether this pandemic scourge of influenza, as it occurred in 1889-90, could be caused by the same bacillus as these strictly localized or house epidemics or endemics.

Since the discovery of Pfeiffer's bacillus we ought to be able to decide this question absolutely and without difficulty. But as a matter of fact we find that bacteriological examinations are in many of these cases neglected, and we possess positive evidence, therefore, in only a few instances. The smaller epidemics of 1893-94 were certainly of the same nature as the great epidemic of 1889-90, for this has been demonstrated both clinically and bacteriologically. That it did not again increase to such a pandemic may have been due to the fact that the soil was not favorable, the greater number of people, at least, still retaining a certain degree of immunity. I am inclined to accept the view of Leichtenstern, that there exists a pandemic influenza caused by Pfeiffer's bacillus and also an epidemico-endemic influenza of identical nature which develops after the pandemic infection has run its course, being caused by the germs left by the latter. This idea is furthermore corroborated by the explanation which I have given below of chronic influenza, namely, the extraordinarily long period during which the influenza bacilli may exist in the secretions of the patient.

The occurrence of various forms of catarrhal fever, which are often called grippe or influenza by physicians and laymen, is something altogether different. Sporadic cases of coryza and bronchial catarrh should never be mistaken for influenza, although the symptoms of influenza may here be imitated in an exquisite manner. I have examined a whole series of such cases, but have never been able in a single instance to demonstrate Pfeiffer's influenza bacillus. It is very important, therefore, that we should strictly separate these cases of pseudo-influenza in their etiological relations from true influenza.

Etiology.

That influenza is a contagious disease there is no doubt, and it can therefore be spread only by human intercourse. The examples

in which its dissemination has taken place solely through contact with other patients are many. It is, however, also possible that its dissemination may take place by seemingly healthy persons, for the reason that a person may have the symptoms of only a slight catarrh, and yet be suffering from influenza, and because, on the other hand, one may be still the carrier of influenza bacilli a long time after he has apparently recovered.

Opposed to the assumption that influenza is contagious, many still hold to the miasmatic theory of its nature; and a third school avoids many difficulties by the conception that it is a miasmatico-contagious disease. The theory of a miasm is, of course, based on the presumption that the infectious germ has an ectogenous existence. The studies of the bacillus of influenza make this to a high degree improbable, and the manner of dissemination of the disease seems to me opposed to the fact that miasmatic infection is necessary. Nevertheless, we cannot probably deny that when influenza first attacked man the germ must have been of a miasmatic nature. On this question there have been extensive differences of opinion; but many authors, writing during the height of the pandemic, have deferred discussion of the question to a later period, holding that a decision could be arrived at only after the bacillus of influenza had been isolated and its characteristics had been demonstrated; and now, after we have discovered the bacillus of influenza, the opinion again finds expression that we ought to return to the practical study of the pandemic. Some authors, as we have said, are believers in a miasm, others are contagionists, and a third group leans to the theory of the miasmatico-contagious nature of the disease. In the latter method of infection there is still another subdivision made, according as the germs are believed to produce their effect chiefly by direct transmission (contagion), or to act as a miasmatic poison. We shall do well in studying the mode of dissemination, in the following pages, to leave aside the old denominations, and to investigate more carefully the manner in which the germs of influenza conduct themselves as regards their entogenous-ectogenous existence.

By the expression miasm we mean the existence and propagation of the germ outside of the human body. In the strictest sense, a miasm can pass into a human being only from its place of abode; each germ which causes a disease must have obtained its infecting qualities outside of the body—properly speaking, must have even originated there also. If we adhere to this definition of the miasmatic poison, it appears very evident that a dissemination of influenza could only exceptionally have taken place in this manner. In proof of the theory of contagion, that is to say, of the carrying of the

materies morbi by human beings from one locality to another, we have an overwhelming number of examples. Some of these will be mentioned below.

The spread of the disease by means of inanimate objects is extremely difficult to prove, as is also the theory that healthy individuals who have come in contact with influenza patients may carry the contagion. For the latter we might cite, as an example, that a physician in Sachsenburg is said to have introduced influenza into the prison. He began treating a patient suffering with influenza at another place, on December 19th, and on December 20th and 24th made his medical rounds in the institution. On December 26th the first symptoms of the disease were observed in a few prisoners. In support of the theory of infection by inanimate objects, an example occurring in the French navy may be mentioned. An officer of the ship *La Bretagne*, which was anchored in December, 1889, in the harbor at Brest, became ill at his home in Brest on December 11th, three days, it is said, after the arrival of a number of packages from Paris, which were first unpacked by the officer. These packages then carried the disease to his ship, while the vessels *Borda* and *Austerlitz*, which were anchored beside this vessel, are said to have escaped the infection.

Another case of infection by the living is furnished in the history of the invasion of the station at the St. Gothard hospice. The watchman who was employed at this hospice during the winter had been to Airolo where influenza extensively raged, and after a visit of some duration returned from here to the hospice. During the month of January not a person ascended the mountain, except this watchman; he remained perfectly well himself, but the other watchman, who had never gone down to the valley at all, became ill with influenza. In this case the infection seemed to have been carried in the clothing. Bäumler says that the first case of disease in Basle occurred in a person who had been engaged in unpacking a bale of merchandise, which had recently arrived from the greatly infected Magazin du Louvre in Paris.

The *incubation period* of influenza could in these and a few other instances be quite definitely determined. In the German collective investigation report some cases are recorded in which the disease originated in a family in consequence of a definite importation, and in a number of instances physicians were able to determine in their own persons how many days after they had visited their first and only case of influenza they themselves were attacked. Based on these observations, the period of incubation was declared to be from two to six days in length. Very rarely it was as brief as one or two days.

One reporter believed that the incubation period might be only half a day, as he was stricken with influenza on the night following his visit to the first influenza patient. It is quite possible, however, that he had previously been exposed to contagion without being aware of it. The longest period that has positively been determined is seventeen days.

Paul L. Friedrich reports numerous cases in which the origin of the epidemic was clearly determined by accurate observations. Thus, the inhabitants of Rosenberg, in the district of Heiligenheil (Königsberg), were indebted for their epidemic to a sailor returning from Dantzic. In Lubeck, the first case was with certainty traced to the porter of a hotel, who had been in close communication with various patrons of the house; his illness was followed within a few days by that of ten of the servants. In Hadersleben (Sleswick), a Swedish steamer hailing from Dantzic brought the first patients, from whom the plague rapidly spread. In two of the districts of Silesia two persons arriving from Hamburg were the proven carriers of the disease germ. In Kiestrup, a soldier on furlough arrived from Flensburg on the 20th of December, and became ill on the 22d; his illness was followed on the 23d by that of his mother, who was the first one in the village to have influenza, and on the same day his father also sickened. The first case in Silesia was that of a student who had arrived from Kiel, which was already infected, on the 15th of December; the second was also that of a student, who had arrived on the 17th of December from Leipsic, where the disease had already appeared.

In Strasbourg a lady, who had come from Paris, was taken ill in a hotel; a servant in this house was the first person to have influenza in the city. In the village of Elbersdorf a recruit absent on leave, in Wurzbach a pharmacist who had come from Erlangen, in Muhlberg a man from the neighborhood of Gera, which had been infected for two weeks, were ascertained with certainty to be the first cases of this disease and the sources of further infection. In Lucka the first patient suffering from influenza was a traveller from Berlin; after him the family of the hotel-keeper with whom he lodged became ill, and only after this were cases of influenza noticed in the village. In Zeulenroda a merchant sick with influenza arrived on the 20th of December from Berlin; the first cases in the village appeared in his family, and after that other persons were attacked in the village. In Meisenheim (Coblentz) but one house, situated on a farm where there lived only a few families in isolated houses, to which a soldier returning home from his garrison brought the disease, was visited by influenza; all the members of

the family in this house became ill, the other houses remaining free.

In the governmental district of Frankfort the disease made its appearance simultaneously in the families of two large landed proprietors, who lived miles apart in the country, but who had both been in Berlin about the same time, and had come into contact with persons suffering from influenza. The members of a family, living altogether secluded in the country near Königsberg, became ill immediately after the arrival of a guest from the infected city of Königsberg.

In Eubingheim (Baden) a merchant, who a few days previously had been on business in Mannheim where the influenza already prevailed, became ill with the disease on the 23d of December; on the 24th of December his wife and two children became ill—these three patients were the first cases in Eubingheim; after this the influenza spread over the whole village within a few days.

The son of a tenant in the neighborhood of Boxberg (Baden) was taken with influenza in the garrison at Würzburg, and came home on leave of absence; two days later all the members of his family became ill with influenza in short succession; the farm itself and the entire neighborhood had up to that time remained free from the disease.

The first patient in Ettlingen was an elderly gentleman, who, after returning from Berlin four days previously, where he had spent four days, had been stricken by the disease on the 11th of December. Three days later his daughter, who had nursed him, became ill, and three days after this second illness the female servant of the house. The latter was taken to the hospital, and was placed in a ward where another girl lay, who was suffering from some slight surgical affection. This other girl became ill on the third day following the reception of the patient having the influenza, with undoubted symptoms of this disease.

A domain lying in the district of Saarburg, aside from the main routes of travel and many kilometres distant from any town, and whose inhabitants had but slight intercourse with the neighborhood, remained altogether free from the disease during the true influenza epidemic. In the middle of February, when the plague had nearly died out in that part of the world, a servant from a mountain village in which the influenza was still raging arrived at the domain. This man became ill on the day following his arrival, and four days later four other servants who lived together with the patient in the same house were attacked.

Quite noteworthy are also a few experiences gathered in the garrison towns of the German army. For the conditions of intercourse could be much more closely observed among the troops than is as a rule

possible among the civil population. In the Eighth Company of the 137th Regiment which had its headquarters in one of the fortifications of Strasbourg, the first case of influenza was reported on January 4th, 1890, while the other companies of the battalion, which was in garrison in Strasbourg itself, had already been visited by the disease on the 24th and 28th of December, 1889. That first case in the fort was in the person of the orderly sergeant of the company, who daily visited the city for the purpose of distributing the parole, and who had had intercourse with influenza patients. From this time the epidemic spread throughout the fort. An artilleryman of the 13th battalion received a pass to Tübingen, and there visited relations who were suffering from influenza; on his return he met a comrade of his battalion. Both of these were the first ones of the battalion who were taken ill with the influenza; a third case followed in the barrack of the soldier first infected. On the following day there occurred thirteen cases of illness in the already infected barrack, and three in the room which had been first infected. A cavalry captain of the garrison at Pasewalk returned home from Berlin suffering with influenza; nothing was known of influenza in the village at that time. After the captain the chief staff physician, who had been treating him, became ill, and then the sergeant of cavalry of the squadron, whose presence the captain of horse had commanded. Next the wife and child of the chief physician of staff, and a gentleman with whom the latter had relations, were attacked. From this time the epidemic became universal.

Many instances have been reported, however, in which the evidence of direct contagion is wanting. The traditions of former epidemics also are that influenza was characterized especially by the rapid spread from one country to another, and by the sudden appearance of the disease in isolated places. This belief was seemingly strengthened in the great epidemic of 1889–90, as the sudden appearance at isolated spots was so striking that it was thought the germs of the disease had suddenly descended like a cloud out of the higher air strata. When it was known that a number of cases of influenza had broken out in one place or another, and other villages which were closely situated near by had been spared, the impression was produced that the germs of the disease had fallen to the earth in local showers, as it were. When, however, we analyze more carefully the beginning of the individual cases of illness, we are convinced that the disease was introduced in every instance by human beings coming from an infected locality. When once the disease was introduced in a place it often spread with great rapidity, but a lightning-like diffusion, such as is often described, has in reality never been observed. The appearance of the

epidemic almost at the same moment among a vast number of inhabitants of a city can only be explained by the fact that there were many single foci and that the infection spread from each of these many centres simultaneously. This mode of dissemination was mentioned as probable in the older English literature, and it has also been demonstrated positively in the recent epidemic.

Bäumler narrates how the disease was introduced into the inn on the Felsberg in the Black Forest (four thousand one hundred and fifty feet above the sea). The inn-keeper had acquired the disease himself in Freiburg and brought it home with him. Then his sister, who was nursing him, sickened; then the servant girl, who nursed the latter; the male servants working in the open air and the rest of the household, who were kept away from the sick-room purposely, escaped.

There are also many very instructive examples of the importation of influenza into prisons. Kirn states that in the state prison at Freiburg, of three hundred and ten prisoners in cells, thirty per cent. became ill; of those working together in the general work-rooms and in the hospital fifty per cent.; of the servants who in part lived in the city, seventy per cent.

Dr. Vanselow, in his reports on the female prison at Cologne, says that the first case was that of a female watcher who had spent two days away from the prison. Her assistant became ill two days later, and the epidemic then rapidly increased in the prison. In the insane asylum at Erlangen there occurred for the first eighteen days cases of the disease only among the staff who had come in contact with the outer world, but afterwards cases of the disease were also observed among the patients.

Here, therefore, we see that among the inmates of closed institutions, those were attacked first who were in communication with the outer world. In monasteries this is particularly noticeable; those which were strictly isolated from the outer world escaped the pest even in the midst of an infected city. In Luoco Pio Trivulcio in Milan, containing four hundred and eighty inmates, there were only four cases of the disease; on the other hand, eight cases occurred among the thirty servants. Alancisi writes of the epidemic of 1708 that the houses and the prisons of the inquisition were spared by the influenza.

In the last epidemic the fact was positively determined that influenza broke out on vessels only after it had been imported from the land. On board of the *St. Germain*, a passenger who embarked at Santander brought the disease with him, which then spread to more than one hundred and fifty-four passengers and forty-seven sailors.

Klas Linroth records that the epidemic originated in the middle of November, 1889, at Stockholm, and spread from there first to places which are connected with it by railroad. On December 20th, the epidemic had visited 108 out of 129 places having railroads, that is 84 per cent., but only 47 of 94 places without railroads, that is, 50 per cent. The plague visited Lapland much later, and it never advanced more rapidly than the means of intercourse permitted man to travel.

It had been previously argued in favor of the miasmatic nature of influenza that persons became ill under such circumstances as seemingly made direct contagion impossible. As a prominent example of this kind, an occurrence which took place on April 3d, 1833, is recorded. The influenza was raging in Devonshire, and while the frigate *Stag* was near this coast, it was driven back by a wind; within half an hour, it is said forty, after two hours sixty, and on the following day one hundred and sixty cases of sickness occurred among the sailors. Proof is wanting that there could not have been some communication previously with the land, for example, through the pilot.

Ripperger endeavors to prove the possibility of ectogenous growth of the influenza germ indirectly, a method which is by no means so convincing as the direct observation made use of for proving contagion. He lays great value on the observation that the number of those attacked by the disease, if this has become very large soon after the outbreak of the epidemic, does not increase steadily, nor is it even maintained for any length of time at the same height. Ripperger employed for the investigation of this question the record of the daily reception of influenza patients in the public hospital at Cologne, the reports of Bäumler concerning the medical clinic of Freiburg, the statistics of admissions to the army hospital and the two general hospitals in Munich, and the daily reports of illness among the employees of the Bavarian state railroads. A study of this material showed in the first place that individual cases of illness precede for a longer or shorter time the full establishment of the epidemic. Then it was seen that the number of cases of sickness will suddenly rise, to fall again as a rule on the following day; and again rise, either on the next or the following day, occasionally later, usually to a still greater height than at first. This is again followed by a sudden fall, then again a rise, until the highest point is attained. The descending curve is similar to the ascending, but only as a general rule somewhat less abrupt, and therefore occupying a somewhat longer period for its completion. The epidemic does not disappear at once but declines as it began, sporadic cases occurring at the end as in the beginning.

That this is not due to chance is shown by the substantial agreement in all the collected statistics.

Ripperger asserts that these exacerbations and remissions in the number of daily cases positively militate against the view of a purely contagious element. He lays stress on the fact that we cannot look for such remissions in a contagious disease but rather for a steady increase in geometric progression, and so believes himself justified in assuming an ectogenous growth of the microorganisms. The germ is taken up by a number of persons, and is then again eliminated from the human body in one way or another. Accordingly we may assume two propositions, either the increase of the disease germ takes place outside of the human body, that is it is ectogenous, or, while this has already been accomplished in the human body, the disease germs are yet obliged to pass through an ectogenous stage in order to regain their infectious properties. The time required for this ectogenic growth, or perhaps only increase in virulence, would explain the remission in the number of cases on the first, second, or third day. Each infected individual would then himself be infectious, but only in an indirect manner; for every infected person carries the germs of the disease within himself and disposes of them; but persons in his vicinity are more likely to become infected after the germ has passed through its ectogenous stage than those who do not live in the near neighborhood.

Rollo Russel made a very interesting experiment to explain the origin of the influenza epidemic in 1889-90. He started with the fact that great inundations occurred in China in 1888 by the overflowing of the Yellow River. It is said that 1,700,000 persons were drowned at this time, and immense regions were undoubtedly inundated. Six months later similar enormous floods occurred in Manchuria. As a result of this calamity this locality was visited by a great famine in the summer of 1889; cholera also appeared, and during the winter another plague caused great perturbation among the inhabitants. During the summer the flooded portions dried up and were covered with the yellow dust, which had been deposited as slime by the Hoang-ho. The dry winds now drove this dust in such quantities into the air that the sun was obscured. Thus it would seem probable that the innumerable organic germs from the Yellow River might have been carried over a great extent of country.

The question as to the influence of the seasons and the weather on the prevalence of grippe has naturally been frequently discussed. As to the *seasons*, we find that epidemics have occurred in every month; more often, it is true, in the winter than in the summer. Hirsch prepared a table of all influenza epidemics with the exception

of the last one, and if we add to it the last pandemic, we obtain the percentage of epidemics which occurred in the single months, as follows: January, 14.38 per cent.; February, 10.86 per cent.; March, 8.94 per cent.; April, 7.03 per cent.; May, 6.71 per cent.; June, 5.43 per cent.; July, 6.07 per cent.; August, 4.47 per cent.; September, 7.67 per cent.; October, 7.67 per cent.; November, 8.96 per cent.; December, 11.82 per cent. The preponderance of epidemics in the winter months is made quite evident from the above. It is undoubtedly true that the influenza finds then the most favorable conditions for its dissemination. It is not possible, however, to determine from this the time of origin of the epidemic, especially as we are ignorant of the locality and under what conditions the first case occurred. We must, of course, bear in mind also that diseases of the respiratory apparatus are notably more frequent, when unfavorable climatic conditions are present. We agree with Hirsch, that the maximum frequency of catarrhal diseases of the respiratory organs is found in the higher and highest latitudes, but that unfavorable conditions of the weather in equatorial and subtropical regions may also determine the occurrence of these diseases.

The *atmospheric conditions* must therefore certainly exert a great influence on the dissemination of grippe, but we cannot as yet say what special meteorological conditions are favorable to the spread of influenza. High barometric pressure, dryness of the air, absence of precipitation, fog, will not in themselves account for the appearance of an epidemic in all cases. The only conclusion which may be permitted is that influenza may spread at all times and in all weathers; that, however, it is most easily disseminated under those conditions in which the respiratory organs are most severely taxed, and therefore are most prone to become diseased. Assmann's observation is worthy of record, to wit, that in the great pandemic of November and December, 1889, a very unusual drought was present in the whole of Eastern and Central Europe, throughout Europe a protecting covering of snow was absent, and everywhere low-lying clouds and high atmospheric pressure were observed. We cannot, however, at the present time at least, predict the appearance of an influenza epidemic from any existing atmospheric conditions.

Still more difficult is it to discover any influence on the disease exerted by *telluric conditions*. When a peculiar susceptibility of the individual races in former epidemics is spoken of—for example, that the white race was attacked in Rio de Janeiro, the mixed races less frequently, the black race not at all, and that at other times exactly the reverse is asserted—we must remember that the habits and conditions of life were very different in these different races, and such

are undoubtedly of much greater influence in determining intection than are purely racial susceptibilities.

Another question is, whether any special *age* predisposes to influenza. In the pandemic of 1889–90, the assertion was often made that children under five or six years of age were as a rule less susceptible to the disease. Some observers hold that infants are nearly immune. Flesch reports a series of cases in which nursing mothers were attacked by influenza while the children at the breast escaped, an observation which is corroborated by Fehling, who writes that not one of the nursing children in his wards took the disease, notwithstanding that they were nursed by mothers suffering with influenza. Leichtenstern also remarks upon the slight susceptibility to infection during the first year of life. The statistics of past epidemics do not give us any special information concerning the relative susceptibility at different ages, and the attempt has therefore been made to collect such statistics concerning the ages of patients admitted to hospital. Up to a certain point such statistics are useful, if we take into account at the same time the average age of hospital patients as shown by the statistics of admission for a series of years. An interesting table of this kind is given us by Leichtenstern. His hospital material included four hundred and thirty-nine influenza patients, and these he carefully grouped together according to age.

Age.	Influenza admissions.	General average of admissions.
Under 10 years.....	0.9 per cent.	0.7 per cent
10 to 20 "	14.7 "	8.8 "
20 " 30 "	40.3 "	27.5 "
30 " 40 "	19.1 "	23.3 "
40 " 50 "	10.1 "	15.7 "
50 " 60 "	7.4 "	12.3 "
60 " 70 "	5.3 "	8.9 "
70 " 80 "	1.7 "	2.6 "
Above 80 "	0.4 "	0.2 "

We see from this compilation that persons from twenty to forty years of age were attacked by influenza in greater numbers than those in the earlier or later years of life.

In other observations these proportions do not obtain in the same manner. Auerbach has collected the statistics of 200 families distributed throughout the whole city of Cologne. He found that 149 of these families (75 per cent.) were attacked. In these 235 persons were ill—59 men, 95 women, and 81 children. The large number of women was due to the illness of the female servants. Should we count each family as consisting on an average of 6 individuals, we find that 20 per cent. were taken with the disease. Comby in Paris men-

tions that only the new-born were noticeably insusceptible to influenza, that, on the other hand, children up to fifteen years of age were attacked in the proportion of 40 per cent., adults in the proportion of 60 per cent. Danchez also reports that in families in which all the adults became ill, the little children usually all escaped.

In most of the schools at Bordeaux the older children were first and most frequently attacked. Of the 242 male and female teachers in these 41 schools, 153 (61.7 per cent.) were attacked by the influenza. Very few reports mention the contrary fact. As a general rule, children up to five or six years of age at any rate seem to have been very little affected, while older children were no less susceptible than adults. Among 47,000 cases of influenza treated by physicians in Bavaria, the various ages were as follows:

1 year.	2–5.	6–10.	11–15.	16–20.	21–30.
1.5 per cent.	5.4 per cent.	6.6 per cent.	7.3 per cent.	11.4 per cent.	22.2 per cent.

31–40.	41–50.	51–60.	61–70.	71–80.	Above 80.
19.3 per cent.	12.6 per cent.	7.7 per cent.	3.6 per cent.	2.0 per cent.	0.5 per cent.

The statistics of age of the 2,856 influenza patients among the employees of the Bavarian government railroads (22.5 per cent. of the whole personnel) show that the greater number of patients were between thirty and fifty years of age:

Under 30 years.	30–39.	40–49.	50–59.	60 and over.
20.9 per cent.	24.6 per cent.	24.3 per cent.	21.9 per cent.	14.6 per cent.

This is particularly interesting for the reason that it has been statistically proven that the employees over fifty years of age usually suffer more from other diseases.

Leubuscher notes in his observations on the influenza epidemic in Jena that there the proportion of cases in the individual age classes did not correspond with the figures met with in other localities. There was much less sickness in proportion among children than among adults, and this peculiarity was especially marked in very young children. He met with only six cases of the disease up to the end of the first year of life, and the older children also showed a remarkably low percentage of sickness. According to inquiries made of the director of the local gymnasium, only thirty-four scholars out of a total attendance of two hundred and thirty were absent at the commencement of school in January, this being at the height of the epidemic. On the whole, we may place the proportion of cases among children up to twelve years of age compared with that of the adults at one to twenty.

Lent has collected the following statistics of the incidence of influ-

enza on school children in Cologne. The statistics for the city itself were as follows:

		Attendance.	Ill of influenza.
Class I.	13 to 14 years of age....	3,002	1,015 = 33.8 per cent.
" II.	11 " 12 " "	5,737	1,835 = 31.9 "
" III.	10 years of age	3,701	1,130 = 30.5 "
" IV.	9 " "	3,590	930 = 25.9 "
" V.	8 " "	2,929	822 = 28.0 "
" VI.	7 " "	3,388	758 = 22.3 "

The following were the results of inquiries concerning the public schools in the suburbs of Cologne:

		Attendance.	Ill of influenza.
Class I.	13 to 14 years of age....	1,609	689 = 42.9 per cent.
" II.	11 " 12 " "	2,885	1,094 = 37.9 "
" III.	10 years of age	1,683	626 = 37.1 "
" IV.	9 " "	1,758	552 = 31.4 "
" V.	8 " "	1,771	502 = 28.2 "
" VI.	7 " "	1,938	510 = 26.3 "

Two interesting facts are revealed by these figures: (1) The increase of the disease with the age; (2) the greater affection of the country population in contradistinction to that of the cities. Here we must take into account that the children in the country had usually to walk a greater distance to school.

As regards the school children of Lausanne, Comby tells us that out of 3,411 school children, 1,840 contracted influenza, from which we may see that children of the school age, from six to sixteen years, were attacked in great numbers.

Occupation.—When we compare the statistics of the last pandemic concerning the influence of vocation, we see in the first place that those first and chiefly were attacked whose occupation compelled them to remain in the open air. This was shown especially by Neidhardt, who studied the influenza epidemic in the Grand Duchy of Hesse. His conclusions, however, were disputed by others. Thus, the prejudicial influence of exposure to the open air was not supported by the statistics of railroad employees in Saxony. Of those who were employed in the outdoor service, thirty-two per cent. became ill; of those employed in office work on the other hand, forty per cent. The statistics of the local benefit societies in Plauen show that the percentage of the sick among farm hands and builders was not greater than that among the members of other benefit societies who worked indoors. In Schwarzenberg the laborers in the forest, who were working in the open air all day, were affected less than others, and there was no sickness whatever in some forest districts. Lancereaux, of Paris, states that most of the railroad employees who

suffered from influenza were those engaged in office work, and not those who worked in the open air. The preponderance of influenza patients among the factory hands may be seen from a table prepared by Ripperger:

A—In the Open Air.

Occupation.	Per cent. attacked.
Workmen and laborers of Niederbayern	7
Railway officials in Amberg	9
Peasants in Niederbayern	11.7
Workmen in the Salzach-Correction	20

B—In Closed Rooms.

Slag mills in St. Jugbert	15
Cotton mill in Bamberg	20
Cotton mill in Bayreuth	33
Sugar factory in Bayreuth	36
Aniline works in Ludwigshafen	38.8
Cotton mill in Zweibrücken	50
Tinware factory in Amberg	60
Factory in Schweinfurth	62
Gun factory in Amberg	70
Gold beaters in Stockach	80

Many peculiar records of how individual classes of occupation have fared are obviously to be explained by the fact that the infection manifested its action in very different degrees. Thus, among the workmen on the Baltic ship-canal only those became ill who lived in the town of Rendsburg; those who had been housed in barracks outside of the city were not affected. The 438 lead workers of Rookhope, which is situated in a lonely valley in Durham, all remained perfectly free from the disease during the three epidemics of 1889-92.

In England only 8 cases of influenza occurred in four places among the 415 inhabitants of the 51 lightships and 20 lighthouses along the English coast.

Some occupations are said to afford protection against influenza. Thus workmen in tanneries, chloride of lime, tar, cement, sulphuric-acid, glass, and coke works are said to have escaped the disease with extraordinary frequency.

We shall be compelled perhaps to agree with Leichtenstern in his conclusion that "occupation and social position only in so far exert an influence on the frequency of the disease as certain occupations and positions in life lead to more or less contact with travellers."

Very remarkable is the proportionately small number of soldiers affected, at least in the Prussian army, where, according to the official record, the epidemic from its beginning to its end attacked only 101.5 per thousand of the entire forces.

Bacteriology.

While in all places where bacteriological examinations were made different microorganisms were found in the products of influenza, the specific character of which could not be demonstrated, this investigation assumed an entirely new phase in consequence of the labors of Pfeiffer at the Institute for Infectious Diseases in Berlin.

Some previous observers unquestionably caught a glimpse of this small bacillus, though without recognizing its peculiarities. For example, during the extensive epidemic of influenza the district physician Vanselow, of Cologne, repeatedly observed and demonstrated the small bacilli in microscopic preparations. In 1891, in my paper on influenza pneumonia, I likewise mentioned a small bacillus, and stated that I had found an extremely small microorganism in two cases of influenza pneumonia. One of these cases had a rapid course though otherwise uncomplicated, but terminated fatally in a short time, with symptoms of pronounced exhaustion. From one of the pneumonic foci I obtained, during life, some bloody serum by direct aspiration of the affected lung. The microscopic examination of this serum showed some scanty streptococci. Plate and streak cultures upon agar yielded streptococci and staphylococci, while upon one of the agar plates kept at the temperature of the body there were found cultures which upon microscopic examination showed between the still present blood corpuscles the small bacilli in addition to streptococci. When further attempts were made to cultivate the small bacillus from this plate, the organism disappeared and only streptococci remained.

Another case of influenza pneumonia was carefully examined at the time by Danco and myself, and reported in 1890 by Danco in a dissertation. The patient in question had been infected in the hospital by his neighbor who was suffering from a severe attack of influenza pneumonia. The former patient fell sick on December 24th, and died on January 6th. At the autopsy the right lower lobe was found consolidated throughout. The spleen was enlarged to double its normal size. Immediately after death some material for bacteriological examination was taken from the cadaver with a Pravaz syringe, with the following result: From the pneumonic focus three inoculations were made upon gelatin, two of which remained sterile and one furnished streptococci. From the heart three inoculations were made upon gelatin, all of which remained sterile at the temperature of the body. From the spleen three cultures were made upon agar and one upon gelatin. Upon the surface of one of the agar cultures kept at

the temperature of the body, some sparse, round, small colonies developed, all of which consisted of very small cocci. The second agar plate was similar, while the third and the gelatin culture remained sterile. During the autopsy, which was performed on the same day, two gelatin cultures were made from the spleen and remained absolutely sterile. A stick culture having a bloody color was made in gelatin; this stick culture, having shown no change after some time, was re-examined by being removed from the gelatin and spread over the surface of prepared blood serum. Having been kept at the temperature of the body, this surface showed extremely minute droplets having a bright and colorless appearance. They consisted of an exceedingly small bacillus. I did not succeed in continuing the culture upon agar or other preparations of blood serum, so that I wrote at the time that we had to deal with a very remarkable small bacillus of a most ephemeral character, and that the possibility was certainly not excluded that it was in some way related to influenza.

In January, 1890, Babes of Bucharest also examined a number of influenza patients and the bodies of those dead of the disease. Although complications were present in most cases, he was able to demonstrate that in the greater number of instances exceedingly fine diplobacteria and short bacilli predominated in the sputum. He noticed them within the cells and also in large numbers outside of them, and subsequently did not hesitate to assert that he at that time had seen Pfeiffer's bacilli and had described them as preponderating in the sputum.

Furthermore Kirchner discovered a small microorganism during his investigations which he published in 1890. It was in the sputum that he first discovered this microorganism, which he had not known before and which since then he never failed to find in any bronchial secretion derived from influenza patients. He interprets it as a diplococcus, decidedly smaller than the staphylococcus pyogenes and the well-known streptococci of suppuration and of erysipelas. Pfeiffer, in the spring of 1890, by staining Kirchner's preparations with carbol fuchsin disclosed very slender bacilli in enormous quantities, a photograph of which Kirchner appended to his paper.

These findings in Kirchner's preparations at once gave a definite direction to Pfeiffer's investigations. When on November 30th, 1891, the first cases of influenza were diagnosed in the wards of the Institute for Infectious Diseases, Pfeiffer immediately made numerous preparations from the sputum of the patients. Again the slender bacilli were found in surprising numbers. Thus it was natural that his attention became concentrated upon this microorganism. Pfeiffer started with the idea that influenza may spread over the earth in the

form of a pandemic in a manner unequalled by any other acute infectious disease. If, then, influenza is due to a living virus—which could be presupposed with certainty from the analogy with all other and better known infectious diseases—this germ must be active in large quantities and great concentration during the epidemics. The pronounced contagiousness of influenza rendered it probable that the contagium must stand in intimate relation to the patients and that attention ought to be directed particularly to the sputum; for, in view of the marked tendency of influenza to cause inflammatory and catarrhal processes in the air passages, suspicion pointed chiefly to the sputum as the carrier of the infectious material.

The sputum in influenza presents characteristic peculiarities. It is greenish-yellow in color, viscid, and adhesive, and while in the slighter cases it is derived from the naso-pharynx, a considerable proportion is furnished by the bronchial ramifications as soon as the process has extended to the bronchi or to the pulmonary tissue. As the secretion from the naso-pharynx is contaminated with very numerous species of bacteria, Pfeiffer examined in particular the sputum coming from the bronchi, and this always when quite fresh, immediately after its evacuation. He spread the masses carefully in sterile glass dishes and removed from the middle the purely purulent portions. For staining he employed Löffler's alkaline methylen blue solution, but obtained the best preparations with a very dilute, pale red solution of carbol fuchsin in water. As the stain penetrates very slowly, he allowed the cover-glasses to float for at least five or ten minutes on the surface of the solution. In this way Pfeiffer obtained preparations in which the cell nuclei and the bacteria were stained most intensely and still distinctly, while the ground substance remained perfectly colorless and the cell protoplasm assumed a delicate rose tint.

Pfeiffer states: "In preparations of influenza sputum made under the above-described precautions we find in all recent and complicated cases a single, well-characterized species of bacillus in almost absolutely pure culture and always in surprising numbers. The bacilli are situated mostly in the form of nests and swarms in the mucous ground substance of the sputum. They are found also in greater or smaller number in the protoplasm of the pus cells, where they are grouped around the nucleus, without ever penetrating into the nuclear substance. The influenza bacilli have not quite the transverse diameter of the bacilli of mouse septicæmia. Their length, as a rule, is only two to three times their width, though occasionally we discover in the sputum and sometimes in pure cultures longer forms that are to be regarded as short filaments. In older pure cultures of from

three to four days' duration very long filaments may occur; but these are abnormal forms, the first signs of beginning involution. The ends of the influenza bacilli are rounded. Very often we find two particularly short bacilli in close apposition. These are forms of division that are apt to be interpreted as diplococci and undoubtedly have been mistaken for them. The influenza bacilli have no capsule and in a hanging drop exhibit no spontaneous motion. They do not react to Gram's stain. In rather faintly stained specimens we sometimes notice that the poles of the bacilli are more deeply colored than the middle portion."

The examination of dried and fixed cover-glass preparations of sputum is best effected by staining with a dilute solution of fuchsin or carbol fuchsin (*e.g.*, Ziehl's solution twenty times diluted) which is allowed to act according to its concentration (say, ten minutes). The influenza bacilli can also be made visible by other well-known aniline dyes, but not according to Gram's method. These bacteria undoubtedly are among those stained with difficulty; moreover, they are the smallest thus far cultivated. Their thickness, when they are well stained, corresponds about to that of the bacilli of hog erysipelas (mouse septicæmia), but their length is much less. The individuals arranged in pairs greatly resemble the diplococcus lanceolatus; when faintly stained the individual bacillus may also show a vacuole in the middle, thus presenting the appearance of a diplococcus. Longer forms and even filaments composed of several bacilli are met with. We may observe, too, a certain variability in the transverse diameter, so that some individuals now and then hardly differ in size and form from the diplococcus of pneumonia. In general, however, these two species of microorganisms cannot be mistaken for each other. In typical cases the influenza bacilli are so uniform in size and are present in such enormous numbers in the sputum that the bacteriological diagnosis is one of the easiest tasks. Any stray diplococci that may appear are usually at once recognized by their darker color and their greater thickness. This typical picture is found in the sputum of recent influenza bronchitis.

The Cultivation of Influenza Bacilli.

The cultivation of the influenza bacilli, in order to demonstrate that these microorganisms in all cases belong to a distinctly characterized species and therefore should be regarded as specific microbes, proved at first very difficult to the discoverer. Neither in gelatin nor on agar plates, neither aërobically nor anaërobically did he obtain colonies from the bacillus seen under the microscope. He

did not succeed until he spread the sputum or pus from the lung directly upon agar; then at the temperature of the oven there developed extremely delicate, transparent colonies, only visible through a lens, which were densely crowded over the entire surface of the nutrient medium. But it was impossible to effect the propagation of the bacilli on transplanting the colonies from the first medium either upon agar, even under the most varied additions and with different degrees of alkalinity, or upon blood serum or into bouillon. But Pfeiffer noticed that the growth of the influenza bacilli did not succeed even in the first generation when the nutrient medium transferred with them had been largely diluted or when the material containing the bacilli had been washed out with sterile water. Not until Pfeiffer caught blood in sterile vessels, placed it drop by drop upon the surface of obliquely congealed agar tubes, and with it rubbed up a trace of influenza sputum did innumerable colonies of the bacillus develop and flourish. This is the most important discovery of Pfeiffer, by which it thenceforth became possible to produce pure cultures of the influenza bacillus in large quantities and with facility.

This peculiarity of the influenza bacilli is so fundamental that even in the oldest cultures no further adaptation to saprophytic conditions of life has been discovered. Pfeiffer then made further investigations to determine which constituents of the blood contain the substances necessary to the growth of the bacilli. The blood serum, when free from cells and clear, does not contain them, so that the material required must be present in the red corpuscles. From these Pfeiffer obtained a solution of the hæmoglobin by repeated freezing and thawing or by agitation with ether. After evaporation of the ether he passed the very dilute hæmoglobin solution through a filter bed of silicious earth. In this way he obtained a clear almost chemically pure solution of hæmoglobin in 0.6-per-cent. solution of sodium chloride. When a drop of this was placed upon agar and then inoculated with influenza bacilli the colonies developed as plentifully as in the entire blood. This fact left no question that the first cultures which had succeeded directly with the fresh material owed their development to the traces of admixed hæmoglobin.

It might be assumed that the hæmoglobin plays its part in the cultivation of the influenza bacilli by acting as the carrier of oxygen, which element is urgently needed by these microbes; but this does not appear to be the case, for Pfeiffer found by experiment that carbon monoxide hæmoglobin (CO-hæmoglobin), which can neither absorb nor give off oxygen, likewise favors the growth of the bacilli. Even blood-agar which has been heated for an hour to 70° C. fairly

well supports the development, and hæmoglobin coagulated by boiling also permits a notable growth of the bacilli.

Not only the blood of man but also that of different animals, rabbits, guinea-pigs, pigeons, and fish, was used by Pfeiffer, and the same specific effect was produced by each. The growth was particularly luxuriant in the blood of pigeons. Pfeiffer thinks that the explanation lies in the fact that the red blood cells of the pigeon contain large quantities of hæmoglobin and disintegrate readily.

Upon blood-agar the influenza bacilli present the following characteristics: The colonies are minute droplets; when they are closely crowded they are visible only under a lens, though when they are farther apart and few in number they may attain a considerable size, but even then not exceeding the diameter of a small pinhead. The droplets have no tendency to coalesce. When neighboring colonies merge, the contours of the several droplets always remain recognizable. They possess a remarkable, glassy transparency and on microscopical examination appear almost structureless.

The influenza bacilli are strictly aërobic bacteria. In bouillon mixed with blood or spread out in very thin layers, Pfeiffer was able to note a rather plentiful growth. In an atmosphere of hydrogen only extremely minute, sparse colonies develop, which consist of degenerated forms that are barely recognizable as bacilli.

A high temperature is absolutely necessary for the development of the bacilli; at the temperature of the oven and with the use of pigeon's blood they reach the acme of their development at the end of twenty hours. At 43° C. no growth can be detected, though the bacilli do not die at this temperature. Regarding the lower limit, at 30° growth is still luxuriant, but at 29° it begins to be retarded. At 23° to 24° no trace of development can be discovered even after four days, so that the lower temperature limit seems to be at about 26° to 27° C.

Among Pfeiffer's important investigations as to the state of the bacilli under some conditions corresponding to those of the outer world, the following may be specially noted:

1. In drinking-water the influenza bacilli perish very rapidly. When a platinum loop containing a fresh culture was agitated in sterilized tap-water the number of living bacilli after twenty-four hours at the temperature of the room, in the dark, was very small; after eight hours more the whole was sterile.

2. The duration of life in bouillon, on the other hand, is considerable, the bacilli not dying until after from fourteen to eighteen days, and this was the case in the breeding oven as well at the temperature of the room. It is probable that the duration of life of the bacilli is

the same in the sputum, so that the infectiousness continues for at least two weeks.

3. The influenza bacilli are exceedingly sensitive to drying, almost more so than cholera vibrios.

In order to decide this most important question Pfeiffer placed samples of recent blood-agar cultures together with the surrounding blood upon sterile glass surfaces, by means of a platinum loop, and allowed them to dry there. From time to time particles of the dry mass were scraped off and again inoculated upon blood-agar. In proportion as the drying was sudden the death of the bacilli was rapid; when the drying took place at 37° C., the colonies became much scantier even after from five to ten minutes, and after from one to two hours all the bacilli were dead. At the temperature of the room the culture experiments often became negative after eight hours. After twenty hours all the bacilli were dead. Quite similar results were obtained in attempts to cultivate the bacilli from dried influenza sputum. Sputum which when fresh had furnished countless colonies gave only a few after twenty-four hours' drying; after from thirty-six to forty hours it was sterile.

The question whether the bacillus of influenza possesses a persistent form has also been settled by Pfeiffer. Its slight resistance to drying, its death at a temperature of 60° or after the addition of chloroform, are points positively against the existence of spores. Moreover, upon microscopical examination of recent sputum and of pure cultures, nothing was discovered that could be interpreted as pointing to spore formation. From these investigations Pfeiffer draws the following conclusions:

"1. Any development of the influenza bacillus outside the human body, in the ground or in water, is impossible; 2. The spread of influenza by dried and powdered sputum can occur only to a very limited extent; 3. The contagion, as a rule, is conveyed by the recent, still moist secretion from the nasal and bronchial mucous membrane of influenza patients."

According to Pfeiffer's statements, the following method has proved successful in securing pure cultures of the influenza bacillus: "The original material—bronchial sputum or juice from portions of lung infiltrated with bronchopneumonia of influenza—is first finely divided in 1 or 2 c.c. of bouillon until a uniform and only slightly turbid emulsion results. This preliminary dilution has two objects. In the first place, in the succeeding inoculation the number of the transferred germs is sufficiently diminished, so that separate, well-developed colonies may form. Secondly, the hæmoglobin present in the original material is largely diluted, so that the growth of the

bacilli upon media not previously prepared with blood is completely inhibited. This emulsion is transferred by means of platinum loops to blood-agar and, for purposes of control, also to ordinary or glycerin-agar, and distributed as uniformly as possible over the entire surface. The test tubes are then placed in the oven. After twenty-four hours the colonies are seen upon the blood-agar as densely crowded transparent droplets which under the microscope are seen to be composed of very delicate bacilli; while the control tubes either remain sterile or contain merely scattered colonies of other species of bacteria associated with the influenza bacilli, usually streptococci or Fränkel's diplococci."

A peculiar mode of cultivating influenza bacilli has been devised by Nastinkov. He started with the idea that the yolk of hens' eggs was chemically very similar to blood, in that it contained ferric oxide, potassium salts, and phosphate combinations, and that the iron in the blood as well as in yolk of eggs existed in the form of complicated organic compounds. In order to obtain a particularly transparent nutrient medium he dissolved the yolk in alkaline distilled water, the proportion being 5 gm. of a ten-per-cent. solution of caustic soda to 1 litre of distilled water, to which faintly alkaline fluid 100 c.c. of yolk is added. The yolk is freed from surrounding albumen by rolling it over blotting-paper. The yolk solution thus prepared is placed for about two hours in a Koch steam sterilizer, and on the following day when the liquid has settled it is filtered, poured into test tubes, and sterilized in the ordinary way. In the test tube the solution appears greenish with reflected and yellow with transmitted light. The following is the mode of preparing a one-per-cent. yolk-gelatin: Take 1 litre of the yolk solution and 15 to 20 gm. of agar-agar or 80 to 100 gm. of gelatin, boil until completely dissolved, and replace the evaporated water. The opaque mass thus resulting is passed through a Plantamour filter, and, if desired, meat peptone, etc., is added. Nastinkov reports that he has succeeded in obtaining luxuriant cultures upon this medium from the sputum of influenza patients. Owing to the trouble in preparing blood-agar it would be most desirable if such a culture medium could be used, but it does not appear quite certain that the influenza bacilli are to be found upon it regularly.

When pigeon's blood is to be used for the cultivation of the influenza bacilli, the following method will be found the best. The bird is held firmly, one wing is lifted up, and the small feathers are plucked from the axilla. At the point where the large vessels are visible the skin is washed with sublimate solution, for which purpose sterilized cotton is employed. Then follows washing with alcohol, so that an

absolutely sterile and clean surface is secured. Next the vein is divided with small pointed scissors and a sterile test tube is held so that the drops of blood fall directly into it before they touch any other part of the skin or the feathers. When about 1 c.c. of blood has been collected in this manner, it is well stirred in the bottom of the test tube with a platinum loop previously heated and allowed to cool. The blood is thus defibrinated, and is then spread from the tube upon agar plates or upon obliquely congealed agar surfaces, by means of the platinum loop or a platinum brush. This is a troublesome procedure, and the difficulty of preparing a fresh culture medium often prevents the bacteriological examination, because the inoculation from the fresh sputum cannot be made rapidly enough. It would be well, therefore, if the fresh blood could be dispensed with. To this end Voges prepared media with blood taken from men by cupping and preserved upon ice. This investigator even prefers such media to any other. He keeps the blood on ice, thoroughly agitates the serum with the clot, places a few drops in a Petri dish, adds liquid agar at 100°, mixes well, and allows the mass to cool.

The admixture of blood with the media has another drawback besides the technical difficulty, namely, that a number of plates or test tubes are always unfit for use. Despite every care and practice contamination cannot always be avoided. Huber endeavored to overcome this drawback by using Hommel's hæmatogen instead of the hæmoglobin. Huber describes his method with its advantages as follows: Hæmatogen is a dark reddish-brown, turbid liquid with aromatic odor and taste, and having a neutral reaction. When mixed with agar it proves to be not free from germs, and when the attempt is made to sterilize it in a current of steam it coagulates, forming thick, opaque, brown lumps. On the addition, however, of potash lye until the reaction is strongly alkaline it is possible to secure a preparation that remains fluid at 100° C., and, having been freed by filtration from the few albuminous substances precipitated by heat, keeps clear even after repeated steam sterilization. The dark blood-red, germ-free fluid thus obtained is then added to the liquefied agar by means of a sterilized pipette, about 0.5 c.c. for each test tube, but not before it has cooled to 50° or 60°; for at higher temperatures, owing to the lessened alkalinity following the dilution, coagulation again occurs. In this way is obtained a perfectly transparent, blood-red nutrient medium, upon which the influenza bacilli flourish and upon which they have been cultivated uninterruptedly to the seventh generation. The growth is decidedly slower than upon blood-agar; only rarely in from one to two days, usually not until from three to

five, and sometimes not before from eight to ten days after inoculation do we observe on the obliquely congealed surface those typical small, round, non-confluent, clear water-like droplets, usually visible only with a lens, which represent the colonies. These, moreover, grow but slowly and slightly thereafter, and either never or only after a very long time do they reach a size, enabling them to be recognized with the naked eye, as they do, for instance, upon agar prepared with pigeon's blood. On the other hand, their duration of life is materially increased. While according to Pfeiffer's observations blood-agar cultures are usually dead after from fourteen to eighteen days, and a transfer to a fresh medium appears desirable every four or five days, Huber was able successfully to inoculate hæmatogen-agar cultures thirty-five, thirty-eight, and forty days old.

The influenza bacilli flourish also in hæmatogen-agar stick cultures, in spite of their marked need of oxygen. Here, too, the growth is slowed, however; for a fine gray shadow appears in the depression at the earliest after two or three days, usually not until five or six days, and often very much later. This shadow increases quite slowly in density until it finally appears in the red medium as a dark streak which, examined with a lens, is set with round bosses and resembles a young typhoid stick culture, aside from the difference in color. The duration of life of the bacilli is thus still more increased; Huber inoculated four such cultures without a single failure after twenty, thirty-five, forty-two, forty-seven, and sixty-seven days.

In consideration of all this, in the investigation of influenza for purposes of diagnosis, blood-agar unquestionably is to be preferred to hæmatogen-agar, owing to the slight energy of growth of the bacilli upon the latter; but for experimental investigation the new medium, especially the stick culture which it renders possible, seems to be very appropriate by reason of the protracted length of life of the colonies.

Having been instigated to spectroscopic examinations by the beautiful blood-red color of the nutrient medium, Huber convinced himself that oxyhæmoglobin was not present in his hæmatogen-agar, at least not in demonstrable quantity. This finding may serve to corroborate the fact ascertained by Pfeiffer, that the hæmoglobin is the indispensable factor in the development of influenza colonies, not by reason of its acting as carrier of oxygen, but probably owing to its contained iron.

A hæmatogen medium favoring the development of influenza colonies may also be prepared with soda lye, by which it acquires a yellowish-red color. But as a rule so many crystals form within and upon the surface of the agar that the recognition of the colonies is

made far more difficult. Hæmatogen bouillon is likewise suitable for cultivating the bacillus.

Max Richter made various experiments with a view to cultivating the influenza bacilli upon other media than those of Pfeiffer. He could demonstrate a feeble growth upon agar coated with sterilized sputum, sterile bile, or the yolk of pigeons' and hens' eggs. The development was rather luxuriant upon pus when mixed with blood and sterilized by repeated heating to from 60° to 70°, but not upon gonorrhœal pus treated in the same way. Methæmoglobin still containing some unchanged oxyhæmoglobin was also used with success. Hæmatin solutions prepared after Caseneuve's method proved unsuitable. Richter also found the yolk cultures recommended by Nastinkov entirely inappropriate. Strange to say, however, he obtained but a feeble growth by the use of Hommel's hæmatogen after Huber's method described above. His culture experiments also failed when he added veratin, and with reference to the use of Pfeiffer's blood-agar Richter points out that the preparation of the medium requires great exactitude, especially sufficient alkalinity.

Kitasato, in 1892, at Koch's instigation investigated whether it was possible to obtain pure cultures of tubercle bacilli directly from the sputum of tuberculous persons and succeeded with a method Koch had suggested to him for the purpose. To this end the patients were directed to expectorate directly into sterilized double dishes the sputum raised by a true cough, not by hawking. A portion of the sputum is then immediately isolated with sterilized instruments and carefully washed in at least ten successive dishes filled with sterile water. In this way it is possible to eliminate nearly all the other bacteria which have become mixed with the sputum in its passage through the oral cavity. In the last dish the sputum is torn apart under sterile water and from its midst a portion is taken for microscopical examination and for inoculation upon agar. According to Kitasato, the same method suffices for obtaining rapidly a pure culture of influenza bacilli. Such cultures have a specially characteristic appearance. On obliquely congealed glycerin-agar the several colonies manifest themselves as extremely minute points resembling drops of water, which in the first twenty-four hours can be recognized only with a lens, so that on macroscopic inspection such a tube is hardly to be distinguished from a sterile one. Similar cultures have been propagated by Kitasato for ten generations. Numerous small colonies always develop upon the moist agar surface. What is especially notable about them is that they always remain separate, never coalesce, and never form a coherent layer. This is so characteristic as to be alone sufficient to distinguish the influenza

bacilli. Pfeiffer and Beck could not obtain these results, so that it still remains an open question whether Kitasato's glycerin-agar possessed peculiar properties or whether he was deceived by a morphologically very similar bacillus.

At all events it is absolutely essential for the diagnosis of influenza that the nutrient medium made use of should cause the development of the bacilli without any doubt and should never fail. For this reason the best plan will be to follow Pfeiffer's directions for the time being. Most bacteriologists agree in this, that although the first culture may succeed without blood-agar, this medium is necessary for the further culture. Upon it the bacilli grow most luxuriantly and can be propagated *ad libitum*. Only care must be had to transfer them to fresh media after from four to five days, as they reach their height after forty-eight hours and then die rather rapidly. Half an hour's heating of the blood-agar tubes does not make them unfit for cultivation.

When a medium containing hæmoglobin is used, it can be demonstrated that the bacilli still vegetate in the depth of the puncture where the access of air is limited, although they do so far more scantily than with perfect aërobiosis. Under complete exclusion of oxygen growth no longer occurs.

Regarding the viability of the bacilli in the dried state, Kruse confirmed Pfeiffer's findings. After twenty-four hours at the temperature of the room he found but few individuals among millions still viable and few survived after seven hours at 37°. The influence of diffuse daylight greatly hastens their death. Kruse, therefore, is of opinion that infection with influenza bacilli through the dust of the air is as difficult of experimental proof as it is in the case of cholera.

Condition of the Bacilli in the Morbid Secretions of Influenza Patients.

In this question Pfeiffer's fundamental investigations have also proved almost conclusive. The principal results are as follows: In recently attacked and still pyrexial patients the influenza bacilli are found in the viscid, frothy sputum expectorated from the bronchi during violent attacks of cough; there they appear in free swarms embedded in the mucous ground substance of the sputum, while the pus cells contain the specific bacteria only in small numbers. As the disease advances the microscopical appearance of the sputum changes in a characteristic manner. The number of free influenza bacilli decreases, while the pus cells are actually packed with the delicate bacilli.

Subsequent to the acute stage of the influenza catarrh and during

convalescence the great majority of the bacilli are in the interior of the pus cells. The bacteria also present distinct signs of degeneration at that time; they become very slender, break down, stain with difficulty, and can no longer be cultivated.

In some convalescents from influenza whose recovery is unusually protracted, the explanation of this fact is found in the persistence of the bacilli for weeks after the attack, and they can be demonstrated in large numbers in some of the particles coughed up, especially in the morning.

While Pfeiffer was able to demonstrate these bacilli in the sputum in every case of influenza, he never found them in the blood. In numerous investigations of severe and slight cases of influenza, in which daily from ten to twenty drops of blood were inoculated upon agar, every specimen remained sterile. Not a single influenza colony could ever be made to develop. This fact corresponds with the microscopic findings in sections of tissue. In two instances only did Pfeiffer see the influenza bacilli in the interior of small veins. In both cases, however, these veins adjoined tissue that was completely filled with bacilli. The possibility of their transportation by the blood current, however, cannot be absolutely denied, for Pfeiffer succeeded several times in cultivating isolated influenza colonies from the substance of the spleen and kidneys.

The presence of the bacilli in the secretions of the respiratory organs has since been uniformly confirmed in many investigations covering a large number of individual cases. As Pfeiffer stated in his first communication, he was able to find them in uncomplicated cases in absolutely pure culture and usually in enormous quantities. When influenza attacks persons whose bronchi are affected with some other disease, *e.g.*, phthisical patients with cavities, it is natural to find in the sputum also other microorganisms in varying quantities.

In the secretion of the larynx and trachea there is usually a mixture of different bacteria, among which, however, the influenza bacillus predominates. In cases of influenza pneumonia the foreign admixtures in the bronchi become progressively sparser; in the smaller bronchioles and the pulmonary tissue the influenza bacillus alone remains. In the bronchi the bacilli lie in immense masses upon and between the destroyed epithelium, only here and there penetrating into the submucous tissue. At these points the pus cells are actually overwhelmed with influenza bacilli. This is particularly the case in the central portions of the inflammatory lobular foci. But they also penetrate the pulmonary tissue and get as far as the pleura. In two cases of empyema after influenza Pfeiffer found influenza bacilli exclusively in the false membranes.

Huber has confirmed Pfeiffer's statements in two small epidemics in the year 1893. In five sporadic cases, however, he was unable to demonstrate influenza bacilli either under the microscope or by culture. Still, in these recent cases he failed to examine the nasal secretion, and hence the possibility is by no means excluded that the true morbid process had its seat there. In the epidemic cases Huber found in the sputum, which was yellowish-green, viscid, and nummular, that the influenza bacilli were present in enormous masses and in almost pure culture. He himself admits that in eight other cases in which the process was quite recent and acute, the sputum, scanty and expectorated with difficulty, contained innumerable and various bacteria which possibly may have overshadowed the influenza bacillus. But when he examined the secretion of the mucosa of the nasopharynx in five of these cases, he found the typical bacillus in three.

Nastinkov secured a pure culture of the bacillus from the sputum in twenty cases of influenza examined by him, and Klein likewise demonstrated Pfeiffer's bacilli in the bronchial sputum from forty-three cases of influenza. He also found them in the oral secretion and observed that they gradually disappeared as the patients recovered.

In cases of influenza pneumonia, at the height of the disease, Beck found the bacilli in pure culture in the sputum, very often enclosed in cells. He states that they persisted during convalescence and even after that could be found for a long period in some cases, when at times they suddenly disappeared. Of special bacteriological interest was the case of a man with sarcoma of the lower maxilla, who died suddenly. He had fever but there was no expectoration. At the autopsy the microscopical demonstration of a pure culture of influenza bacilli in the purulent plug of a medium-sized bronchus permitted the diagnosis of influenza which had not been previously suspected.

Among the first confirmations of Pfeiffer's discoveries that of Weichselbaum is of particular importance. He reported in 1892 six autopsies on influenza cases. In all of these he could demonstrate the influenza bacilli in sections of the bronchopneumonic foci. They were situated partly within, partly without the leucocytes and the alveolar epithelia. In the recent cases they were extremely numerous, in the older cases they were more scanty. Weichselbaum demonstrated the same bacilli also in two cases, the autopsy of which had been made some time previously, by staining portions of the bronchopneumonic foci which had been preserved in alcohol. In some cases he found pneumococci associated, but in pronounced

lobular pneumonia the influenza bacilli were present in pure culture. Similar results were obtained by Babes, A. Pfuhl, Albu, Neisser, Borgardt, and Kruse.

The long persistence of the influenza bacilli in the sputum was demonstrated by Kruse in two cases. In one patient he found the bacilli in the sputum four months after the onset of the disease and ten weeks after the termination of the epidemic; of course, the number of the specific bacteria was then much less than in recent cases. A change in their peculiarities, however, was then no more to be discovered than when the bacteria had been cultivated for an equal length of time upon artificial culture media.

In direct connection with the observation of the patients in the Friedrich-Wilhelms-Stift at Bonn, the present writer made an investigation regarding the occurrence of the influenza bacilli, from which may be deduced many conclusions of epidemiological interest and of importance regarding the course of influenza as well as of mixed infections. We shall revert to the results of these investigations in a later section. Here it will suffice to state that the findings agree perfectly with those obtained by Pfeiffer and Kruse. It is quite remarkable that in some cases the bacilli may still be found in the sputum when the patient is apparently restored to health, and that on the other hand they can no longer be found in spite of careful examination in cases presenting alternating improvement and exacerbations and that they then suddenly reappear; and that in other patients again—for instance, in those with bronchiectases—the bacilli could be demonstrated post mortem, while they failed to appear in the sputum during life. One of the cases is of interest, moreover, in that the sputum contained large numbers of influenza bacilli, but the attack of influenza did not occur until the day following the demonstration. This calls to mind a noteworthy case observed by Zaeslein at Genoa, in which cholera bacilli were accidentally found in the intestinal dejections, though the cholera attack began afterwards.

When influenza reappeared in Freiburg in 1893–94, Bäumler succeeded in demonstrating the presence of Pfeiffer's bacilli in the third case. This is all the more remarkable as the patients were not at first suspected of suffering from influenza. After the disease was thus carried into the hospital a number of different patients were affected with it, and in some of these hospital infections the influenza bacilli were likewise demonstrated. In a few cases he also succeeded in finding the bacilli in the sputum as late as four weeks from the onset of the disease, in the course of advanced convalescence.

In the Institute for Infectious Diseases in Berlin, according to Wassermann, the investigation covered many hundreds of sputa, and

the result was that the influenza bacilli were discovered in large numbers at the time of the epidemic of 1893-94, and more rarely after it had run its course. In the non-epidemic period the microorganisms were discovered now and then in large masses in the secretions of some patients; every one of these attacks could be traced back to the time of the epidemic.

Influenza Bacilli in the Blood and the Various Organs.

Pfeiffer's bacilli have been found quite exceptionally in the blood. The discoverer himself observed them in sections in the blood-vessels of such tissue only as was completely infiltrated with bacilli. All the experiments made by him with a view of obtaining the bacilli by culture from the blood were negative in their results. From this fact he concludes that as a rule the specific microorganisms do not circulate in the blood during the attack of influenza. As these bacilli, however, develop with the greatest facility upon blood-agar, the conditions would appear extremely favorable for obtaining a luxuriant growth of any contained bacilli after spreading the blood upon the surface of the medium.

At the time of the influenza epidemic in Naples in the year 1890, Kruse, aided by Pansini and Pasquale, made extensive examinations of the blood. At that time the view prevailed that the presence of the bacilli in the blood was a matter of importance, especially in cases in which the symptoms pointed particularly to the nervous system or to other organs. The above-named investigators examined the blood in fifty cases of influenza, from the earliest stages onward. With all due precautions they collected from the patients from three to fifteen drops of blood upon liquefied gelatin, mixed it with agar, poured it upon Petri dishes, and kept it at a temperature of from 36° to 37° C. The result was absolutely negative, even when the dishes remained in the oven for ten days.

While this alone renders it very improbable that the bacilli are transported in the blood current, we have the additional fact that the microbes were found only in exceptional instances in other organs. Pfeiffer succeeded a few times in cultivating isolated colonies from the spleen and kidney obtained at autopsies. I found the bacillus once only in the spleen of a man dead of influenza. A. Pfuhl claims to have found the bacilli in the brain.

At the same time with Pfeiffer's first report Canon had published the results obtained by him in the examination of twenty influenza patients. In nearly all cases he found one and the same microorganism in the blood. He stained these in cover-glass preparations by

allowing the blood film to dry in the air and then exposing it for five minutes to the effect of absolute alcohol. The stain consisted of a concentrated watery solution of methylen blue and a solution of eosin. According to the description, the organism, colored blue, is found sometimes in larger numbers, but as a rule only sparsely and after prolonged search. It may appear as a small diplococcus, or else, when more deeply stained, as a short bacillus. In six cases Canon found this organism in groups of from five to fifty individuals. In these six cases the blood was taken during a fall of temperature. In most instances the preparation of the specimen was conjoined with inoculation of the blood upon agar and bouillon. The cultures were repeatedly injected into mice, with negative results. Canon asserted that this microorganism occurred in all influenza patients, and since it was not found in blood from other sources and was a bacillus thus far practically unknown, he thought it stood in direct relation to influenza. He also stated that Koch had inspected his preparations and had considered them identical with Pfeiffer's bacillus.

Subsequently, however, Canon concluded that these cultures were not of the influenza bacillus, but in six later cases he cultivated from the blood a bacillus which he asserted to have been Pfeiffer's bacillus. An extremely laborious examination of the blood was required in order to find the bacillus in it. Whether this really was Pfeiffer's bacillus must remain an open question. The small bacilli found by him in the centrifugalized urinary sediment have also not been positively identified as influenza bacilli. On the strength of these rather inconclusive investigations, Canon believes that he had not to deal with an accidental admixture with the blood of isolated bacilli from the respiratory passages but with a true propagation in the blood. He explains the clinical forms of influenza in the following manner: 1. The influenza bacilli reach the air passages, where they find a favorable nidus—the catarrhal form of the disease; 2. The bacilli develop but sparsely in the air passages but profusely in the blood—the nervous form; 3. The bacilli develop luxuriantly in both of these locations—the grave form with pronounced catarrhal and general symptoms.

Pfeiffer believes that Canon's idea is erroneous, for he convinced himself by personal investigation that most cultures started by Canon from the blood remained sterile, while four later cultures did not contain any influenza bacilli but only other microbes. Canon's microscopic blood preparations, however, contained small bacilli which resembled those of Pfeiffer.

Another difficulty in the question of the influenza bacillus was raised by Bruschettini. He began by taking the blood from the

brachial vein of influenza patients, especially those who were in the acute febrile stage. Then he permitted the bacteria to develop in the same blood kept at the temperature of 37° C., and in this way he discovered a bacillus which is devoid of spontaneous motion and grows well upon the ordinary media, but much better upon human and rabbit's blood, or upon blood serum mixed with gelatin. It grows also, though more sparsely, in gelatin at 22° C. The bacillus is anaërobic. It stains only faintly with simple aniline solutions, but does so fairly well with Löffler's solution and with dilute Ziehl's solution. It does not react to Gram's method. It is polymorphous and, according to the stage of its development and the nutrient medium employed, it may present as a diplococcus, a streptococcus, or a bacillus. In glycerin-agar it appears as a coccus, in rabbit's blood as a small bacillus with rounded ends, two or more individuals being united in chains. It is difficult to divest one's self of the suspicion that these were not pure cultures. The discoverer of this bacillus also investigated its pathogenic qualities and reported the remarkable fact that he always found agar and bouillon cultures without effect, while blood cultures were harmless to guinea-pigs and rabbits, but proved pathogenic to dogs and white mice. He found the morbid picture produced in the rabbit after injection of the culture into the trachea to be very similar to that of influenza in man. There result fever, mucous catarrh of the nose, dyspnœa, and death after from twelve to fifteen days, with symptoms of bronchitis and pneumonia. The inoculated microorganisms were found in large numbers in the blood and the bronchial secretion of these animals. These bacteria also had a poisonous effect when acting through the blood. An injection into the veins caused death; one into the pleura, into the pericardium, and into the peritoneum of rabbits produced acute inflammation of these serous membranes and often even the death of the animal. The bacillus discovered by Bruschettini was specially tested by Bombicci with a view of discovering whether it can stand desiccation, and whether, if introduced into the respiratory organs, it is able to cause influenza in animals. He states that he infected animals by making them inhale the dried masses of bacilli. The bacillus resisted rapid drying for about a month, slow drying for seventy days. Bruschettini also made some experiments regarding immunization by his bacillus; these will be discussed elsewhere.

Pfeiffer and Beck subsequently showed that Bruschettini must have experimented mainly with streptococci, whose virulence was mitigated, and moreover his culture methods were marked by serious errors.

Kitasato and Babes described bacilli more or less similar to that

of Pfeiffer, but the essential and fundamental difference consists in the fact that those writers were able to cultivate their bacilli upon glycerin-agar or ordinary media, and this not only in the first generation, which is possible also with the influenza bacillus, but to the tenth and later generations. Knowing as we do the peculiarities of Pfeiffer's influenza bacillus, we are forced to the conclusion that all these investigators had to deal with other bacteria. They committed the same error as did all the bacteriologists who made their investigations during the first influenza epidemic. In this way alone can we explain the fact that even capable investigators failed to find a trace of Pfeiffer's bacillus during that epidemic, while, on the other hand, nothing developed upon their media but diplococci and streptococci.

Kruse, Pansini, and Pasquale assume that in the nervous form of influenza we would be most likely to find the cause of the disease in the morbid products and in the blood. In fifty specimens of blood examined in various phases of the affection they were unable to demonstrate the presence of microscopic microorganisms. From the sputum they were able to cultivate, besides the streptococcus and Fränkel-Weichselbaum's coccus, several other bacteria, especially a number of cocci which from their morphological appearances they looked upon as varieties of the Fränkel-Weichselbaum coccus but which did not prove pathogenic to horses and dogs.

Animal Experiments.

Although experience teaches that our domestic animals are not subject to influenza, experiments have been made to transfer pure cultures of influenza bacilli to animals. Pfeiffer's experiments were absolutely negative with mice, rats, guinea-pigs, rabbits, swine, dogs, and cats. On the other hand, it is interesting to note that he succeeded in producing infectious processes in monkeys.

Pfeiffer injected into the trachea of a monkey a flake of influenza sputum, the size of a pin's head, which the microscope had shown to contain a pure culture of the bacillus, the flake having been well divided in 1 c.c. of bouillon. The animal died after having presented but slight symptoms, and at the post-mortem a walnut-sized abscess was found adjoining the trachea at the point of injection; besides, some portions of the lung were atelectatic and the afferent bronchi were filled with greenish-yellow pus. The pus of the abscess as well as that of the bronchi remained sterile when spread upon agar. The microscopical examination revealed in the pus only very few influenza bacilli which stained poorly, but no other microorganisms. Three

other monkeys were inoculated with dilutions of these bacilli which had been cultivated for twenty-four hours upon blood-agar; the injections were made directly into the lungs through the thoracic wall. The reaction of the animals consisted in fever which began in from twenty to thirty hours after the inoculation, had a remittent character, and ended by lysis; the evening temperatures becoming progressively lower from day to day. The animals also had a cough but they recovered, and when they were reinoculated after two weeks they reacted much more mildly. Another monkey received some of the culture into the nose, any injury of the mucosa being avoided; the same evening fever set in and continued for several days. A fifth monkey received into the trachea an injection of three entire influenza cultures diluted with 1 c.c. of bouillon. The same evening the temperature rose rapidly to 39.2°. The next day the monkey was very sick, the temperature began to fall, and death occurred forty-eight hours after the injection, with symptoms of profound prostration and a temperature of 32.2°. This experiment is of great importance because the injected microorganisms had not multiplied, corresponding anatomical changes consequently had not occurred, and death therefore was due to the toxic products of the influenza bacilli.

Pfeiffer made additional experiments concerning the toxicity of the influenza bacilli and found that rabbits were very sensitive to the poison of grippe. After an intravenous injection of a twenty-four hours' culture of the bacilli upon blood-agar diluted with 1 c.c. of bouillon he invariably observed the characteristic morbid picture. The animals, which were quite lively immediately after the injection, presented the first symptoms of poisoning after from one and a half to two hours. A marked dyspnœa set in, together with very notable muscular weakness. The rabbits, breathing with difficulty, lay on the ground with loosely extended extremities. Still there were no symptoms of actual paralysis, for when the animals were lifted up they moved their legs in apparently normal manner. The body temperature showed a marked febrile reaction, the temperature rising to 41° C. After five or six hours the animals gradually became more lively, resumed their normal position, and began to move like healthy rabbits. After twenty-four hours only a slight rise of temperature indicated the past attack of poisoning.

When the dose is doubled or trebled the animals perish with very similar but more marked symptoms. The temperature falls ante mortem to less than 36° C. The necropsy is on the whole negative. There is some hyperæmia of the lungs, the spleen is small, but there is nothing else of note. It is to be specially remarked that the

microscopical and bacteriological examination of the blood and of the various organs showed only a quite exceptional growth of influenza bacilli; hence there was evidently no multiplication of the injected bacteria, but rather their death in the rabbit's body was rapid.

The same symptoms of poisoning could be produced in rabbits by the intravenous injection of like doses of cultures killed by chloroform. Consequently the influenza cultures contain a virulent poison that produces in rabbits dyspnœa and muscular weakness resembling paralysis, that is, a morbid picture presenting marked analogy with the well-known symptoms peculiar to influenza in man.

Guinea-pigs and mice bear relatively enormous doses of the influenza bacilli.

In the course of his investigations with the influenza bacilli Nastinkov made eighteen animal experiments. Pure cultures grown according to his method upon yolk-peptone-agar were used for the injections which were made into the trachea, the lungs, the auricular vein, and the peritoneum. In one experiment the heart valves were injured mechanically by a sound introduced through the common carotid artery to the floor of the left ventricle. Twelve of the animals were rabbits, two guinea-pigs. In order to reduce the resisting power of the animals ether or alcohol was injected into the trachea or the lungs. For one of the experiments a rabbit was used which had been infected with tuberculosis. In all of the cases in which pure cultures were injected the animals showed some reaction. Healthy and robust animals bore the injections better than the weak and sick. The lymphatic glands showed hyperplasia and cheesy degeneration. The lungs presented signs of inflammation and the liver was enlarged. Altogether, these three organs were most seriously affected.

Kruse likewise studied the effect of influenza bacilli upon the animal body by means of a large number of experiments. Like Pfeiffer he found that while it was possible to kill the animals ordinarily used for experiments by large doses of the bacilli, yet these would not develop in them. Rabbits are most susceptible; with them a reaction may be obtained with comparatively small doses (one-fifth of an agar colony). When these animals are inoculated subcutaneously a local swelling results, and in from one to two weeks this becomes a consistent nodule which on section resembles a potato. After a further lapse of time the nodule softens and ultimately we find thick pus like that common in rabbits. The smaller nodules are absorbed, the larger ulcerate. The influenza bacilli can usually be demonstrated under the microscope only during the first few days, but they are evidently degenerated; sometimes, however, a culture will suc-

ceed even after weeks. This local affection in rabbits, which is not mentioned by Pfeiffer, appears to Kruse to be quite characteristic of influenza bacilli, as he has not met with it under other conditions. Histological examination shows that we have to deal with dense purulent infiltration of the subcutaneous tissue which, contrary to what occurs in ordinary suppuration, is followed by liquefaction of the tissue very late and sometimes not at all. No analogy can be recognized with the processes caused by influenza pneumonia in the lungs.

In order to explain the effect of local infection of the respiratory organs upon the general organism, it is necessary to assume that the influenza bacilli produce a toxin or several toxins which exert an influence preëminently upon the central nervous system. Of course, in the case of some affections, the presence of the bacilli as such in other organs than the lungs will be effective. Thus Přibram calls attention to some grave cerebral symptoms for which he inculpates the immigration of influenza bacilli into the meninges. Pfuhl's labors likewise point to the demonstration of the bacilli in the brain, in blood preparations, and in the fluid of the ventricles during encephalitis and meningitis. The cases to be discussed in connection with the nervous symptoms of influenza prove the multiplicity of these manifestations, leading as they do to intense, prolonged morbid features in central and peripheral portions of the nervous system. These considerations induced Cantani, Jr., to study, under Pfeiffer's direction, how the modus of infection is brought about, and to ascertain the nature of the toxin, together with its poisonous action. The influenza toxin obviously acts preeminently upon the brain; for this reason Cantani investigated especially the influence of the bacilli upon this organ. He first convinced himself that trephining did not injure the animals, and therefore ascribed the results of his experiments to bacterial action alone. He succeeded in killing rabbits by the injection of relatively small doses of living influenza bacilli. The first symptom presented was a rise of temperature (to 42° C.). Along with this was observed a steadily increasing dyspnœa; paralysis also set in, beginning with the hind legs and spreading forwards over the whole body. The animals lay helpless on one side, unable to raise either head or ears. This condition continued for hours, and finally the animals died. When a non-lethal dose was used the symptom complex was less pronounced, and then a chronic meningitis frequently developed; this was sometimes fatal, but often ended in recovery. The minimal fatal dose varied. With moderately virulent cultures the animals died from 0.5 mgm. of a twenty-hours' blood-agar culture. When very virulent, however, very small quantities sufficed; for instance, two

loops of the culture diluted with 1 c.c. of bouillon killed the animals in twenty-four hours.

The necropsy of the dead animals showed all the signs of a marked intoxication. A bloody exudate was often present in the abdominal cavity, and there were hyperæmia of the peritoneum, spleen, liver, kidneys, and lungs, nephritis, and pericarditis. Cantani, however, was never able to demonstrate influenza bacteria in the peritoneal exudate, in the blood, or in the organs. The bacilli were present, on the other hand, in the gelatinous œdema at the place of trepanation, in the fluid of the ventricles, in the brain substance (acute encephalitis), so that the bacilli seem unquestionably to have multiplied in the brain. They appeared to spread by preference through the lymph vessels. The influenza bacilli were also demonstrated in the spinal cord. They seemed to immigrate into the gray substance through the central canal. A considerable increase in virulence could be produced by the admixture of a brain emulsion. The bacteria, therefore, appeared to find a most favorable nutrient medium in the brain substance.

The pure toxin effect was studied by Cantani by means of the injection of dead bacteria into the brain. When the animals were inoculated subdurally with fatal quantities of the toxin, the temperature rose, often to 42° in from ten to twelve hours; then it fell until death ensued. When the dose was not fatal, the febrile condition continued for about two days and then the temperature returned to the normal. Paralytic symptoms were especially prominent. Occasionally the animals recovered even after complete paralysis. At the same time the animals emaciated extremely. With every repetition of the intoxication the receptivity of the animal to the poison was very materially increased, so that an acquired immunity was out of the question. With these intoxications likewise there were found hyperæmia of the meninges and hemorrhages into the brain substance.

Demonstration of the Influenza Bacilli.

The right of Pfeiffer's influenza bacillus to be regarded as the specific cause of this disease is based, in the first place, upon the fact that it is found regularly in clinically well-characterized cases of influenza. It has already been shown at length that a large number of reliable bacteriologists completely agree upon this point. When we seek the explanation why previous to Pfeiffer's investigations this small bacillus was not found by most observers, we find it partly in the fact that it is more difficult to stain than other bacteria.

A second necessary proof of the specific character of the influenza

bacillus is that it is absent in all other diseases. That it had not been found before Pfeiffer's time in other diseases of the air passages would prove very little, since at that time but few persons had seen it even in influenza; but also since the publication of Pfeiffer's discovery the most reliable observers have confirmed the statement that the organism is not to be found in simple bronchitis, in suppurative affections of the respiratory organs, or in tuberculosis uncomplicated with influenza; and in this connection a special interest attaches to the observations of Kruse and Finkler, according to which Pfeiffer's bacilli appeared and disappeared in other diseases of the air passages parallel with the occurrence and evanescence of influenza symptoms.

Does the microscopical finding alone suffice for the demonstration of the influenza bacilli? Under certain conditions this question may be answered affirmatively. Any one who has occupied himself largely with these bacilli will rarely err when he sees them in a sputum preparation. He is perfectly justified in speaking of a typical influenza sputum, and there are many cases in which the clinical manifestations correspond to true influenza and the bacilli are found in the sputum in pure culture. In the expectoration the bacilli often have a characteristic arrangement, lying together in long trains, so that they have been compared to schools of fish, and often they are present in such enormous masses that they cover the entire field of view. It is most desirable, however, to establish the identity of the bacilli by culture, if every doubt is to be excluded, for this method leads to the certain demonstration of the influenza bacilli, often more rapidly than the microscopical examination. The culture succeeds only, according to Pfeiffer's statements, at the higher temperatures, either by taking the material containing the bacilli, such as sputum or the pus from cavities, and spreading it directly over the surface of the ordinary media, or when the original material has been diluted, by using the surface of media which have been covered with blood or hæmoglobin. A very reliable method is that devised by Kruse, as follows: Take several test tubes containing two-per-cent. nutrient agar, pour off the water of condensation accumulated at the bottom, liquefy the agar, and pour it hot into Petri dishes. By not closing the latter but allowing them to cool under a bell glass greater evaporation is obtained and the subsequent occurrence of water of condensation is prevented. The pigeon blood is then spread by means of a previously heated platinum brush over the surface, and in the same manner the material to be tested for influenza is applied either directly or after dilution with sterile bouillon. Some material is then taken from the finished plate with a previously heated brush and spread

over a second plate coated with blood, and so on. In this way any desired dilution is obtained. This method has material advantages over that employed by Pfeiffer, who spread the material over obliquely congealed agar surfaces. Among many hundreds of foreign colonies it is easy, according to Kruse's method, to find even a single influenza colony and to isolate it, especially as the latter is extremely characteristic. Such colonies usually appear perfectly transparent, colorless, and structureless; only under certain conditions they have a yellowish tinge in the centre, that is, when the layer of blood corpuscles is rather thick on the plate and the age of the culture is somewhat advanced. Of great importance, moreover, is the lustre due to the curvature of the colony, whose contour may be regular or irregular. While a confluence of the several cultures with each other or with foreign colonies is possible, the line of separation can always be discerned under the microscope. When these several peculiarities are borne in mind, influenza colonies will hardly be confounded with others. The diagnosis becomes sometimes more difficult with the naked eye, although it can, as a rule, be made even when the plates are plentifully covered. The perfectly transparent, dewdrop appearance is occasionally found with other species of bacterial colonies (diplococci), and on the other hand, as stated above, the influenza colonies are not always absolutely transparent and colorless.

The mode of cultivation here described proves sufficient for the diagnosis in many cases in which the microscope fails. The latter may be the case either when the bacilli are too sparse, perhaps partly degenerated, and enclosed in cells, or when numerous other, morphologically similar bacteria are present, as in the secretion from the mouth and the neighboring cavities. Thus Kruse, for instance, succeeded in a case of phthisis, in isolating the bacilli three months after the onset of an attack of influenza, although it had been impossible for several weeks to demonstrate them under the microscope. A different interpretation is probably required for the following case, likewise that of a phthisical patient. The sputum had been examined for months, but in vain, both by the microscope and by cultivation, for the presence of influenza bacilli. After the death of the patient plates were inoculated at the autopsy with different portions of the lungs, with the unexpected result that influenza bacilli in pure culture developed from the pus of a large cavity. During life the patient had presented no definite signs of an attack of influenza, only the loss of strength in the terminal period was remarkably rapid.

The further cultivation of the bacilli from the plates offers no difficulties when Pfeiffer's directions are observed. In late genera-

tions the addition of blood to the agar is always necessary in order to secure development of the colonies. The transfer is best made at intervals of four days; after six days Kruse often met with failures, although at times a positive result could be secured even after twelve days. As the use of pigeon blood is quite convenient, Kruse felt no need to search for other nutrient media.

Borgardt lays stress on the necessity of cultivation, since occasionally even the expert may find it difficult to recognize the influenza bacilli, owing to their differences in size and their staining reactions; they may readily be mistaken for diplococci when their ends are more deeply colored than the middle. In his culture experiments he found that well-isolated colonies formed on the plates in twenty-four hours when a properly selected flake of sputum was diluted in sterile bouillon and then applied. When, however, the flake was used directly for inoculation the bacilli developed within a shorter period (twelve to fifteen hours), more luxuriantly, though of course more contaminated with other bacteria.

In only six out of thirty cases R. Grossberger found the influenza colonies so largely predominating that on being inoculated in the usual dilutions upon blood-agar they presented the picture described at the time of epidemics as nearly pure cultures. In the remaining instances other germs developed more or less numerously alongside of the influenza bacilli. The admixture found consisted mainly of diplococci, streptococci, and staphylococci. In pure cultures only the isolated colonies attained the dimensions given by Pfeiffer, and besides they manifested a certain sensitiveness to excessive or deficient alkalinity of the nutrient medium. In mixed culture with staphylococci they attained very uncommon dimensions, however, and prove extremely tolerant of marked differences in alkalinity. A careful investigation convinced Grossberger that in the symbiosis observed by him there was some influence exerted by the bacterial products upon the hæmoglobin which effected such a change in it—whether it was an altered solubility or a chemical change in a more restricted sense—as to make it more readily assimilable by the influenza bacilli. According to this statement, an artificial mixed culture with staphylococci would be apt to produce a gigantic development of the influenza bacilli and consequently would materially facilitate their discovery.

In 1892, Teissier, Roux, and Pittion, of Paris, made bacteriological examinations in grippal diseases and endeavored to isolate microorganisms from the blood and from the urine. In a few cases their results were positive; they found in three instances in the urine and in two in the blood bacteria which are especially stated to have

been polymorphous. This polymorphism consisted in the occurrence of diplobacilli and of long chains (streptobacilli). In bouillon cultures the bacillus was said to appear lancet shaped, resembling the microbe of pneumonia. Upon agar media it was said to resemble the bacillus of typhoid, while on gelatin the culture was more like that of the bacillus coli. It is difficult to repress the thought that this was by no means a pure culture, but that different microorganisms had been under observation. When these authors state that the microorganisms were pathogenic for rabbits; that they produced convulsions, "nervous attacks," vertigo, digestive disturbances, affections of the lungs or of the pericardium, and nephritis; but that the temperature curve presented a certain resemblance to that of influenza in man, it is not possible to form any conclusion as to what variety of bacteria they were dealing with.

A bacillus which is said to present an uncommonly strong resemblance to that of Pfeiffer was described by Canestrini, who found it in the blood in a case of influenza. The likeness to Pfeiffer's bacillus in its morphological features, its mode of development, and its staining reactions was marked, but it flourished well also in anaërobic cultures. This last peculiarity justifies the assumption that the bacillus was not that of Pfeiffer. Pfeiffer and Beck believe also that neither the organism described by Bruschettini nor that of Babes was the one producing influenza. The same authors also reject the statements of Chantemesse, who in conjunction with Cornille injected into the auricular vein of a rabbit a drop of blood from an influenza patient, and subsequently found in the blood of the animal a bacillus which they thought was the same as that of Pfeiffer. Although it is very difficult at the present time to say in which class we should place the bacilli of Kitasato, of Pfuhl and Canon, and of Bruschettini, they must under all circumstances be kept apart from that of Pfeiffer.

There is still another group of investigations in which not new varieties of bacteria but such as were previously known were found in grippal processes and were used in various ways for explaining the different manifestations of influenza. In these investigations, judging from what is thus far known, the question was one of mixed infection, *i.e.*, the association of well-known bacteria with the bacilli of influenza.

One of the first bacteriological reports in the earlier period was that of Seifert, of Würzburg, who stated that streptococci in large numbers were present in the sputum of influenza patients. It was reported from Vienna that in the cases there examined Fränkel's pneumococcus could be uniformly discovered. Jolles found in the

secretions and in the urine of influenza patients numerous micrococci resembling Friendländer's pneumococcus, but their capsules could not be stained. He thought them to be connected with similar organisms which he had found in December, 1889, in the Vienna drinking-water and which were said to have disappeared during the decline of the epidemic. The findings reported by Seifert and Müller in 1883 from Würzburg, in which streptococci in long chains were described, form a transition to the discoveries made in Bonn. Rippert found the streptococcus pyogenes abundantly in the bronchial mucus, in the infiltrated tissue of the inflamed lung, and in the sputum of five cases. Finkler found streptococci in all pneumonic foci of true grippal pneumonia, the material having been secured by aspiration from the living patients, by means of a Pravaz syringe. He found the same organism in the lung and the spleen at six autopsies; once he found staphylococci and once diplococci, but these differed from those of Fränkel. In all these findings, therefore, the ordinary causative agents of pneumonia occupied a subordinate position. On the other hand, Weichselbaum discovered a coccus resembling the diplococcus pneumoniæ in the secretions of febrile influenza patients. Marmorek found no microbes in the blood of influenza patients, but in the purulent bronchial secretion he discovered spherical and lancet-shaped bacteria, short bacilli with a gelatinous capsule, and diplococci. In one case Friedländer's pneumococcus was present. When the process was localized in the lung he found no other organisms than Fränkel's pneumococcus. Diplococci were found, moreover, by Georges and Burgas in the lungs of influenza patients suffering from pneumonia and they obtained the same in pure cultures from portions of the spleen. In the study of secondary morbid conditions during influenza Weichselbaum invariably found the diplococcus. Once a streptococcus was observed in the pus from purulent rhinitis, but the diplococcus appeared in all other conditions—in the urine, in the purulent discharges from the middle ear, in meningitis, in nephritis, and in the intestinal canal of patients who had manifested symptoms of enteritis.

While these investigators, in conformity with their experience, naturally suspected some connection between influenza and the diplococcus, the other authors named above, who had found chiefly streptococci, were inclined rather to connect the latter organism with influenza, particularly because the frequent occurrence of the same microbe was also reported from distant localities. Thus Laveran, of Paris, stated that he had but rarely met with the diplococcus in infectious pneumonia, but that streptococci were regularly present in

the sputum. Bouchard, too, found the streptococcus among other bacteria in cases of influenza; and Babes, besides other bacteria which he described in detail, cultivated a streptococcus that was said to differ materially from the ordinary streptococcus pyogenes. In fatal cases of influenza, however, he had noticed, aside from these streptococci, other bacterial colonies which were connected with each other by peculiar radiating processes. While these earlier observers respectively argued in favor of streptococci and diplococci, others reported observations in which the two species of bacteria were found either simultaneously or in succession, in very numerous cases of influenza.

In seven cases of otitis following influenza Levy found Fränkel's diplococcus six times in pure culture and once the staphylococcus pyogenes albus; in one case of bronchopneumonia aspirated during life, Fränkel's coccus. Levy maintained that, as these microorganisms were found only in complicated cases of influenza, none of them could be the exciting cause, and that there was simply an infection upon a soil prepared by the influenza. According to this author's opinion, several microorganisms are apt to produce the infection both in influenza and in pneumonia.

Prudden examined the sputa and nasal secretion in seven cases. In two of these the sputum contained preponderating masses of the streptococcus, besides some bacteria from the air; in the third case large numbers of Fränkel's diplococcus and of the staphylococcus pyogenes aureus were present. The sputum of six cases of pneumonia following influenza contained diplococcus pneumoniæ, staphylococcus aureus, and streptococcus pyogenes; one case, streptococcus and staphylococcus aureus. No special form of bacteria was found in seven cases of simple influenza.

In the microscopical examination of dry cover-glass preparations from the secretions of the oral, nasal, and pharyngeal cavities Kowalski found no form of microorganisms specific for influenza, nor did he discover any species to be constantly present, only mixtures of bacteria were always demonstrated. By culture he isolated thirty different varieties of saprophytes, several familiar pathogenic germs, and three hitherto unknown organisms. He demonstrated staphylococcus aureus five times; staphylococcus pyogenes albus, four times; diplococcus pneumoniæ Fränkel, twice; streptococcus, once; Friedländer's bacillus pneumoniæ, staphylococcus aureus, albus, and flavus, each once. Among the three unknown varieties Kowalski found one, which he called the gelatin coccus, present seven times, and he says that if this coccus had been constantly found it would have been justifiable to regard it as the exciting cause of influenza.

Klebs discovered in the blood of influenza patients monads measuring 1–1.5 μ which were in active motion, also a larger form (2–3 μ) that moved more sluggishly. Klebs observed these formations at the margin or in the interior of the red blood corpuscles. In a later communication the same author states that he had found in subsequent cases, in the blood and in coagula, resting-forms which by transverse division produce types appearing as diplo- and tetracocci. Klebs says further of these organisms: "Upon the ordinary firm nutrient media they seem to grow with difficulty, so that negative results are usually obtained; but when cultivated with blood they develop readily in bouillon and then resemble Fränkel's pneumococcus, from which they differ, however, by their active motion. Inoculated upon dogs they cause fever, though this is of short duration." Inasmuch as "firm nutrient media" must mean gelatin and agar plates, we note a certain resemblance to microorganism II., whose defective growth upon gelatin plates when inoculated from the blood, as well as its pathogenic action upon dogs, has been proved.

Leyden found in the sputum of grippal croupous pneumonia Fränkel's diplococcus, by means of which he produced septicæmia in rabbits. From one case with loose hepatization of the lung he was able to cultivate a variety of coccus which, inoculated upon rabbits, produced no effect. In another similar lung he discovered four different strepto- and staphylococci.

In his bacteriological examinations of the complications of influenza Drasche reports that he found in the lungs streptococcus pyogenes, diplococcus Fränkel, staphylococcus pyogenes aureus, albus, and flavus once each; in the pleural exudate, pneumococcus Fränkel five times, streptococcus five times, pneumonia bacillus Friedländer once.

In the sputum of the cases examined by him Kirchner found without exception a micrococcus (diplococcus) with oval capsule; it appeared never single but sometimes in chains. He found the same organism alone in pneumonia, in two cases of purulent pleurisy, and in the blood in three cases with severe general symptoms but presenting no localization in the respiratory apparatus. Kirchner believes that the microorganism is not identical with the Fränkel-Weichselbaum diplococcus, nor with the streptococcus pyogenes or erysipelatis. Experimental inoculations upon rabbits gave negative results. Kirchner leaves it an open question whether this diplococcus is the cause of influenza or is characteristic of this disease.

Of these various bacteriological findings the chief interest attaches to those relative to streptococci, diplococci, and Friedländer's pneumobacilli. In this connection it is to be specially noted that these

different species of bacteria occurred by no means regularly in the disease at various localities; on the contrary, that in some places an unquestionable predominance of one species was positively established. Let us see first of all how this relation applies to the streptococcus. Ribbert, of Bonn, found in a large number of post-mortem cases a streptococcus which he held to be identical with the ordinary streptococcus erysipelatis. In two cases the plates inoculated from a lung in a state of lobar disease had remained absolutely sterile. Along with these streptococci he found the staphylococcus pyogenes aureus very sparsely, but never Fränkel's diplococcus pneumoniæ. The diplococcus observed by him in a single instance associated with the streptococcus appeared to be not identical with that of Fränkel.

At the same time and in the same place Finkler pursued an extensive investigation. In forty-five cases of grippal pneumonia he examined the sputum, or material aspirated during life from pneumonic foci, or specimens from the cadaver. In every lung examined he discovered the streptococcus. In one single lung he found a staphylococcus, and a diplococcus which he held to be different from that of Fränkel. So, too, in the examination of pus from two cases of otitis media the streptococcus appeared, in one case in pure culture, in the other associated with the staphylococcus albus. In the sputum likewise the streptococcus was most frequently discovered. In the blood which he had obtained before death from the spleen cultivation demonstrated streptococci and the absence of all other bacteria. In the blood of a cadaver dead of influenza the streptococcus was also found, although there had been no pneumonia. In this connection, however, it is to be particularly noted that of the forty-five cases of pneumonia only two presented the type of lobar fibrinous pneumonia, while the remaining forty-three cases presented the clinical picture of true grippal pneumonia.

In Paris, that is, far from the last-named locality, Vincent and Vaillard obtained similar results at the same time. They examined intestines, blood, and exudates from influenza cadavers, as well as the sputa and pleuritic exudates from the living, and invariably found the streptococcus erysipelatis both on microscopical examination and by cultivation. Duponchel and Laveran found the same organism, but never the diplococcus pneumoniæ. In harmony therewith are also the results of Du Cazal, who in fourteen influenza patients found the streptococcus, and in four cases of pneumonia following influenza always failed to discover the diplococcus.

While we are forced to assume that in the localities named there was an almost exclusive occurrence of streptococci, there are on the other hand a large number of observations which demonstrated the

diplococcus pneumoniæ along with the streptococcus. But it is noteworthy that among these are very many cases in which either streptococci or diplococci alone were present. In this group belong the cases investigated by Netter and Duflocq, of Paris. In ten cases of empyema occurring in the course of influenza Netter demonstrated the streptococcus seven times and the diplococcus pneumoniæ three times. In only two cases both bacteria were present in mixed infection. Similar investigations are reported by Leyden, who found in the sputum of influenza cases in four instances only the diplococcus pneumoniæ, in three only the streptococcus, in ten both diplococcus and staphylococcus. From some of the sputa cultures were made; they showed the diplococcus alone in three cases, the streptococcus alone in two cases, both bacteria mixed in two cases. Zaufal examined two cases of otitis media, one of which contained a pure culture of the streptococcus as demonstrated by cultivation and the inoculation of mice, the other the diplococcus pneumoniæ, likewise in pure culture. Schreiber examined eight cases of otitis media during influenza with the following result: Streptococcus twice, diplococcus twice, staphylococcus in pure culture once, streptococcus and staphylococcus associated twice.

Prudden, of New York, examined seven cases of uncomplicated influenza and found in two the streptococcus pyogenes, and in one the diplococcus pneumoniæ associated with the staphylococcus.

Buchner, of Munich, found in three carefully examined cases of influenzal exudates (two of pleurisy, one of pericarditis) the streptococcus twice and the diplococcus once, in pure culture. Emmerich, of Munich, also found the streptococcus in a case of empyema.

Prior's investigations are noteworthy. He examined the sputa of nine influenza patients; in two of these the diplococcus alone was present, in the others it was associated with the staphylococcus and streptococcus. In the instances in which the three bacteria were conjoined, the diplococcus predominated in four cases; in the other three the staphylococcus was in the majority in two, and in one the streptococcus ranked first. Among twenty additional examinations the diplococcus pneumoniæ was present in eighteen. In fifteen cases he found the three species of coccus conjoined, but in these too the diplococcus predominated. Prior also examined sixteen cases of grippal pneumonia, in which he demonstrated the diplococcus pneumoniæ without exception; in three cases it was the only organism, in seven it was associated with streptococci, in six with streptococci and staphylococci. Aspiration of the spleen yielded in one case diplococci and streptococci, in another a pure culture of streptococci, in a third case streptococci alone. Prior's examinations, however, showed

a certain order in the way in which the different bacteria appeared. In six cases of grippal pneumonia carefully investigated by him, the mutual relation of the bacteria changed markedly and with rapidity. The staphylococci always remained scanty, but the streptococci increased enormously, so that in comparison with them the previously numerous diplococci dwindled, often so quickly that in from six to eight hours the appearance was completely altered in this sense. In two cases in which at first diplococci and streptococci were associated, the latter organism finally presented itself exclusively, a pure culture appearing at once upon the medium. This relation was observed by him so frequently as to lead him to draw special conclusions therefrom. This process becomes all the more important by the fact that in one case it could be demonstrated at the autopsy that this occurrence depended upon the stage of the disease; for the recent foci in the lungs contained chiefly and often exclusively colonies of diplococci, the older and disintegrating ones were occupied by streptococci. Prior therefore maintains that the diplococcus is largely the forerunner of the streptococcus; that the former creates or helps to create conditions under which the latter flourishes best. Many cases differ at the outset in that the diplococcus predominates or is alone present in some, while in others the streptococcus assumes this position. When relapses occur, they are due to the diplococcus. When the disease takes on a grave character the streptococcus will always be found. It appears, moreover, from the aspiration of the various exudates that the streptococcus renders the prognosis worse; thus in pericarditis it was alone present, in grave pleurisy it predominated and subsequently was the sole organism, and in suppurative otitis media it occurred frequently in pure culture. In a patient who had succumbed on the first day of the disease Prior succeeded in finding in the spleen the diplococcus alone, while in patients dying after several days' duration of the affection streptococci predominated in the spleen and often were the only bacteria present. All these facts point to the possibility that the streptococcus follows in the train of the diplococcus, crowds it out, and after its death possesses the faculty of proliferating alone and keeping up the inflammation independently.

Mention should now be made of several investigations in which, contrary to those cited above, the diplococcus pneumoniæ was discovered either alone or in excess in the products of influenza patients.

Levy, of Strasbourg, found in the sputum of influenza patients large masses of the diplococcus pneumoniæ Fränkel, sometimes along with staphylococci and streptococci; among seven cases of purulent otitis media he found it in the secretion in pure culture in six, in the seventh case it was associated with the staphylococcus pyogenes

albus. In the examination of five cases of empyema, of serous pleuritic exudates, and of one seropurulent exudate, he discovered the diplococcus pneumoniæ eight times, only once conjoined with the staphylococcus, and the latter alone but once (serous exudate). In a case of bronchopneumonia likewise he found the diplococcus.

The investigations of Weichselbaum, of Vienna, covered the sputa of twenty-one cases, including one with bronchopneumonia and two in which fibrinous pneumonia developed subsequently; the rest were uncomplicated. Weichselbaum examined the cases not only under the microscope but also by culture and by animal experiments. The sputa were always remarkably rich in bacteria; as a rule one species of coccus predominated and at times was exclusively present. The similarity of these findings to those of Prior is evident. According to Weichselbaum, this occurrence is observed only in fibrinous pneumonia, but not in the ordinary catarrhs of the respiratory organs. The diplococci found by him agreed culturally with those of Fränkel, but showed material differences in animal experiments. When mice and rabbits were inoculated with pure cultures, only one-third of the animals showed the effects which are usually observed after the inoculation of the first generations of the pneumococcus. Weichselbaum found only small numbers of streptococci and staphylococci. In the case of a young man with acute influenza he succeeded in demonstrating the same diplococci in the urine. The same organisms were particularly abundant in material taken from cadavers. The examination covered the bodies of ten persons who had succumbed partly with, partly without complications. In every instance the accessory cavities of the nose, the maxillary and frontal sinuses were completely filled with thin or lumpy pus, invariably containing the diplococci which, inoculated upon animals, always proved extremely virulent. He therefore found the diplococcus in all cases.

Sirena, of Italy, also found the diplococcus pneumoniæ along with other microorganisms in the sputum. Marmorek, of Vienna, cultivated the diplococcus constantly and preëminently in seven uncomplicated cases of influenza. The organism found by him flourished more luxuriantly in the culture but was far less virulent in animal experiments than is usual with the pneumococcus. In France, Germain Sée and Bordas demonstrated the diplococcus pneumoniæ almost regularly in the secretions of the patients and in the pneumonic exudates of the cadaver. Bouchard found the diplococcus in grippal pneumonia, staphylococci in the vesicles of labial herpes accompanying influenza, and streptococci in the bronchial secretion. In Switzerland, Haegler demonstrated the diplococcus by cultivation in ten out of twelve cases of influenza, in the secretion of the

nose and pharynx, in the sputum of pneumonia patients, and in empyema. Krannhals, of Riga, found the diplococcus often associated with streptococci, in each of twenty post-mortem examinations of cases of croupous pneumonia and pleurisy following influenza. Curschmann, of Leipsic, found the staphylococcus constantly in purulent bronchorrhœa during influenza.

The investigations of Friedrich, of Berlin, yielded the staphylococcus albus once in an uncomplicated case, once during beginning secondary inflammatory manifestations, and a staphylococcus resembling the former, which was pathogenic to mice. A streptococcus was found twice, and the diplococcus pneumoniæ twice. The streptococcus, when cultivated, showed differences from that of erysipelas. Its development was more luxuriant, the growth was more pronounced in the depth than at the surface, and the temperature most conducive to it lay between 37° and 40° C. Its slight virulence and power of resistance seemed to justify its differentiation from the streptococcus erysipelatis.

Deligiannis, of Athens, instituted a bacteriological examination of eight cases of influenza and, for purposes of control, of two cases of true pneumonia. Aside from the bacterium termo and the staphylococcus pyogenes aureus, he attached special importance to the discovery of an hourglass bacterium. He applied this term to a bacterium in clusters composed of paired cocci connected in hourglass shape. He based his differentiation of these bacteria from diplococci upon their form (hourglass), their distribution (clusters), and a peculiar staining-reaction. Babes, of Bucharest, frequently found a pathogenic streptococcus which differs in several respects from the ordinary streptococcus. In one case he discovered a microorganism which resembled the lancet-shaped sputum bacterium. Babes also found, besides the staphylococcus pyogenes aureus, some zooglœa forms and diplobacteria, and two species which proved pathogenic to mice and rabbits. Petruschky, of Königsberg, discovered in some cultures made from the blood of influenza patients streptococci differing from each other by their development and reaction. In a case of cerebral abscess during influenza he obtained by plate culture an acid-forming streptococcus. Petruschky's different cocci all responded to Gram's stain and under the microscope proved to be arranged in pairs, in straight short rows.

Arloing discovered in a bouillon culture from the blood of an influenza patient at the height of the disease a rounded, delicate microorganism occurring isolated or in pairs in small groups surrounded by a frothy mass. This microbe differed from all hitherto known and proved pathogenic to rabbits.

Kirchner, of Hanover, examined partly the nasal secretion and the sputum, partly the sputum and the blood, and partly the pleuritic exudate of twenty-nine cases of influenza. Every sputum without exception contained a micrococcus, which was extremely small, was surrounded by an oval capsule, and was double, never single, and while it exceptionally appeared in chains it did not lose its character of a diplococcus. The same microorganism was found in the pneumonia cases, unaccompanied by other microbes; also in the pleuritic exudate which was purulent in two instances. In three cases of grave general infection without marked localization in the respiratory apparatus Kirchner was able to demonstrate these organisms also in the blood. The diplococcus found by him was not identical with Fränkel's pneumococcus, nor with streptococcus pyogenes, nor with streptococcus erysipelatis. Kirchner did not attempt to decide whether the diplococcus described by him was characteristic of influenza or possibly the exciting cause of the disease.

Fischel, of Prague, isolated from the blood of a woman suffering with influenza two species of microorganisms which he declared to be diplococci of a form hitherto unknown and which differed from each other in their growth upon different media and their effect upon animals. Fischel's experiments showed that one of these cocci cultivated by him was not pathogenic for rabbits, dogs, horses, and fowls, while the other species was pathogenic for dogs and horses. He thought the symptoms produced in these animals were similar to, if not identical with those of the distemper to which they are subject. In old sterilized bouillon cultures of this last variety of coccus Friedländer's pneumobacillus and the streptococcus pyogenes develop more luxuriantly than in fresh peptonized meat broth.

These numerous investigations with their well-authenticated results, which have in part been gained by the expenditure of much labor, have by no means lost their value through Pfeiffer's discovery of the specific cause of influenza. The clinical picture of influenza shows great multiformity and the bacteriological findings furnish many points in explanation of this fact. It may be safe to assume that future epidemics will reproduce the same conditions. We shall be forced to revert to the above-described bacteriological findings in the discussion of the several prominent organic affections, of the complications, and especially of the differential diagnosis. While the knowledge of the influenza bacillus has furnished us much information as to the nature of this infectious disease, we may, on the other hand, derive many advantages from the proper appreciation of the accidental bacteria to be met with.

Pathological Anatomy.

Influenza is one of the infectious diseases in which we are struck by the great discrepancy between the clinical appearances and the post-mortem changes. Physicians were surprised at the many-sided picture under which influenza was met with, and it was for this reason that from the beginning the idea prevailed that in this disease a distribution of the infectious agent takes place through the circulation. During the course of the disease the various organs show a marked disturbance of their function. All the more on this account does it strike one that at the post-mortem of a person dying from influenza those changes which were specially to be attributed to influenza do not stand out as very characteristic. Very many of the changes in the various organs were at once looked upon by the pathological anatomist as complications, as accidents which added to the well-known picture of influenza. Despite this fact, there still remain, after the exclusion of a complication, certain appearances which are found quite regularly in cases of influenza. Under this heading the pathological changes which take place in the respiratory tract are first to be mentioned. In the nose and the neighboring nasal cavities, manifold diffuse inflammatory processes have been observed. Babes described swelling and injection of the mucous membranes in these regions, together with a mucopurulent coating, and Weichselbaum, who paid particular attention to the subject, found, exterior to the cavities, at one time thick ofttimes clotted and even thin pus, at another time muco-pus, and less frequently only mucus within the cavities. According to the intensity of the process the mucous membrane was only œdematous, diffusely injected, or showed irregular ecchymoses. According to his observations all the cavities were not as a rule affected. The frontal and superior maxillary cavities were most frequently involved—and then only on one side—whereas the ethmoidal cavities were changed in but a small majority of cases. In other parts of the mucous membrane a departure from the normal conditions of affairs was very frequently absent.

According to the observations of Ribbert a redness of varying intensity in the mucous membrane of the large bronchi, the trachea, and in many cases of the larynx was common to all the cases. This injection was least marked in one of the first observations of Ribbert, which was slightly different, however, in that there existed on the mucous membrane a white mucous froth, whereas as a rule it was covered with a tenacious gray or yellowish-green mucus. Babes had already laid stress upon these inflammatory appearances of the

upper respiratory tract. He was also struck by the tenacious character of the mucus, which appeared now white, then grayish-yellow, and again entirely purulent. Babes further states that at times the bronchi were filled with tenacious mucus of a brown character or with coagulated masses of pus; that the mucous membrane in these parts was markedly hyperæmic and of a brown color. The injection of the mucous membrane will sometimes be found equally distributed over large areas so as to give one the impression of an erysipelatous process. The microscopical examination seems to confirm this impression. One of the first to give us information on the subject was Ribbert, whose writings most fully describe the condition. There existed a very marked cellular infiltration of the mucosa together with an engorgement of the blood-vessels; this infiltration spread out between the glands up to the cartilage, and the epithelial cells were loosened to a great extent, the round cells being pressed between. It must be emphasized as an essential appearance that corresponding to this erysipelatous course the catarrhal changes in the mucous membranes show a strong tendency to advance, and they extend from the pharynx and nose to the larynx and trachea, and thence make their way into the bronchi and the substance of the lung; or the trachea and bronchi first appear infected, and the redness and swelling of the mucous membrane then extend to the nose and its surroundings.

The pathological anatomy of the lungs in influenza is of particular interest. At a very early period, the interest of pathological anatomists was directed to these changes, because most cases of influenza which were seen post mortem were in patients who died of pneumonia. At this point it must be remarked that a sharp division exists between the specific grippal pneumonia and inflammations of the lungs which are observed in the course of influenza. The earliest elaborate accounts of this specific influenza pneumonia were given by Finkler and Ribbert of Bonn.

However, at the very beginning of the last epidemic of influenza there existed a certain diversity of opinion upon this subject, when from many sides cases of pneumonia were reported which occupied a prominent part in the post-mortem findings of influenza, but which did not possess the specific character of this disease. Essentially characteristic for the real influenza pneumonia is the following pathological condition: The inflammation occurs in disseminated areas; from these centres the inflammation radiates in many directions, breaks through the lobes of the lung, and constitutes small lobular pneumonias, which though spread over a large area of lung tissue still enclose small aërated patches. For this reason the cut surface

of the lungs presents a checkered appearance, inasmuch as the pneumonic areas are more deeply stained and in the later stages appear hyperæmic. The cut surface of the pneumonic areas themselves is absolutely smooth, sometimes significantly granulated, as it were, never, however, granulated in the manner of a typical fibrinous pneumonia.

The infiltrated areas are not hepatized, but splenicized, so to speak. The forerunner of the inflammation itself is not at all, or only in part of a fibrinous nature. The condition is one of a preponderance of cellular inflammation with an additional partaking of the interstitial tissue. The peculiar mixture of the inflamed with healthy lobular areas explains also the peculiarity of certain clinical physical symptoms. The cellular character of the inflammation, together with the marked tendency to further spreading and development, leads one to look upon the affection as erysipelas of the lungs.

Altogether independent of this description, Pfeiffer also characterized the changes which we find in the lungs of persons who have died of influenza. He also found the lungs to a greater or less extent the seat of pneumonic infiltration, but even to the naked eye essentially different from the uniform lobar hepatization of croupous pneumonia. Without any difficulty he recognized that they are composed of a number of lobular areas which are either separated by aërated tissue or, in part at any rate, merge into one another. In this manner originate the secondary apparently lobar infiltrations, which upon close examination we can recognize, however, as made up of the separate lobular pneumonic areas. Pfeiffer further describes a structure of the single lobular areas. In their centre small pinhead to pea sized parts are separated by a grayish-yellow coloration from the surrounding dark red tissue. Pressure upon the cut surface of the diseased lung shows exuding from the bronchi or from the centre of the infiltrated tissue a yellowish-green, thick, very tenacious pus which at once reminds us of the sputum of an influenza patient. If we follow these events further, we recognize that we are dealing with the lesions of bronchopneumonia, extension of the inflammatory process to the smaller bronchi and thence into the parenchyma of the lung itself. Apart from clinical experience and the deductions which may be made therefrom, this view is based upon the account of the microscopical examination of these lesions by Pfeiffer. He conducted his examination over the entire bronchial tree, beginning at the larynx and extending to the alveoli and by means of his superior staining methods rendered possible not only a recognition of the pathologico-anatomical changes, but also that of the bacteria present in this disease. Pfeiffer hardened his cut sections and embedded

them in celloidin. The thinnest sections may be stained with Löffler's methylene blue, or better still with a diluted Ziehl's solution. In the latter the preparations must remain at least half an hour, and are then to be transferred to absolute alcohol which has been rendered slightly acid by the addition of acetic acid. Here the preparations require close watching. As soon as the original reddish-black color changes to a peculiar red violet the preparations are at once taken out and kept in xylol. Good preparations are distinctly stained and show a carmine tint. By this means the bacteria are intensely stained, and stand out very prominently, the cell protoplasm being stained a faint pink. These directions for staining which have been given to us by Pfeiffer must be strictly followed, and it is a matter of considerable experience and training to be able to so distinguish the various tints as to secure with certainty the excellent pictures of Pfeiffer.

If we follow the fundamental description of Pfeiffer, our attention is at once directed, upon examination of the specimen with the low power, to the bronchi. In the larger bronchial branches the ciliated epithelium is partly destroyed. Some epithelial fragments lie free in the lumen of the bronchus; in other places the epithelium is raised from its base by pus cells. We also see the pus cells collected together in small masses on the apparently intact epithelial edge, where they make for themselves a pathway between the cylindrical cells. They further fill all the cavities which are caused by the falling out of the ciliated epithelium in the epithelial bed, and cover in a much thinner layer the free surface of the same. The capillaries and vesicles in the neighborhood of the bronchi were found by Pfeiffer engorged with blood, the peribronchial connective tissue being studded with wandering cells.

In the smaller bronchi a similar condition was found. Frequently, however, their lumen is entirely filled with a finely granular substance which we must look upon as coagulated mucin, which stains poorly and which encloses within itself numerous pus cells. Within the substance of the lung itself we observe small purulent infiltrations which are arranged in such a manner that in the diseased areas the centre literally swarms with round cells. Here and there the structure of the lung is entirely gone, and in some places there form within such a changed tissue round and sharply defined defects, which give to the sections upon examination with the naked eye a sieve-like appearance. Pfeiffer believes that these defects are caused by very small abscesses.

In the neighborhood of these purulent infiltrations of the lungs the alveoli contain besides the round cells, swollen, pale, or often

pigmented cells which Pfeiffer regards as lung epithelium. If we stain these cells by the method of Weigert, we recognize that fibrin is entirely absent in the central infiltrated areas, and that it exists but sparsely in the outer zones.

Particular value is to be given to these appearances because they point out the typical differences between croupous pneumonia and the pneumonia of influenza; so much so that Pfeiffer says a confounding of these two processes is absolutely excluded by their means. Pfeiffer came to further conclusions by the examination of these parts of the lung with higher powers. The small influenza bacilli described by him now appeared deeply stained and in enormous numbers in the bronchi, upon the epithelial cells as well as between them, being especially heaped up there and rendered more visible by the destruction of the epithelium.

We can discern these bacilli lying in masses under the epithelium, whereas they are seen but singly in the submucous tissue. Both the epithelial cells and the pus cells which lie between them are filled with the small bacilli. The significance of this picture is that we have to deal with a catarrhal suppuration, as it were, which might be compared to the gonorrhœal affections of the urethra and conjunctiva. The explanation of the picture is that the infectious agent irritates both the epithelial cells and the spaces between them, thus leading to hyperæmia of the submucous tissue. Numerous wandering cells now adhere to the walls of the vessels and reach the free surface of the bronchus, there load themselves with the bacilli and thus form the mucopurulent secretion of influenza bronchitis. By means of this high power, we also see how the round cells which fill the lung tissue are overloaded with the influenza bacilli. In the outer zones, the cells containing bacilli are fewer in number.

As far as other microorganisms are concerned, especially streptococci and diplococci, Pfeiffer found nothing even in fresh cases, either in the sections or in the smear preparations. In his explanation of influenza pneumonia, Pfeiffer starts out with the idea that each infiltrated area stands in relation to a diseased bronchus, and that through the medium of the latter the cause of the disease is enabled to reach the substance of the lung. This description is especially based upon changes which are found post mortem when death takes place at the height of the disease. At this time the above-described changes very clearly show the pathologico-anatomical conditions of the lungs in influenza. If we examine the lung at a later period, after the inflammatory process has gone through later stages, then what strikes us most is the formation of abscesses, in consequence of which a few alveolar areas which are entirely filled with

round cells merge into one another and form small, often enough miliary pus areas. In other regions the infiltrated areas in the lung are transformed into cicatricial connective tissue. With the appearance of induration and carnification there appear in such places changes in the substance of the lung which lead to the formation of uniform, hard grayish-red, cartilaginous masses. These regions then project above the level of the lung substance, and are seen upon cross-section to be devoid of air. The alveoli are then filled with masses of a newly formed connective tissue.

This is also the manner in which gangrene of the lungs in influenza is brought about. The influenza infiltration is the primary condition to which is added, in the case of gangrene, a secondary infection by means of inspired mouth bacteria. These, finding a locus minoris resistentiæ in the inflamed lung thrive there. Pfeiffer is also inclined to the belief that the pneumonia of influenza may go over into caseation, as soon as the pneumonic infiltration has established itself in those regions of the lung which previously were the seat of tuberculous or so-called peribronchial nodules. In such lungs Pfeiffer describes, besides those places which have undergone total caseous degeneration and which contain numerous giant cells and tubercle bacilli, other regions which, on account of their uniform infiltration with round cells, remind us of the lesions of grippal pneumonia. According to the researches of Finkler we must conclude that this process of Pfeiffer, which is to be looked upon as a genuine bronchopneumonia, is not the only one which exists in cases of influenza. Instances are also observed in which the mucous membrane of the larger bronchi and trachea shows characteristic changes, but in which the inflammatory appearances in the mucous membrane of the bronchi become less and less evident the deeper we enter into the bronchial branches. Here the link is wanting between pneumonic disease of a cellular character in the lung substance on the one hand, and changes in the bronchi on the other. At any rate, we cannot accept the idea that in such cases the inflammation in the course of the lumen of the bronchi spreads itself into the substance of the lung. There the finest bronchi are found in the centre of cellular infiltration, free from the appearances which Pfeiffer has described. It must be admitted that here there exists another connection between the diseases of the larger bronchi and the lung, so that even without the medium of a direct transmission of the bronchial pus by aspiration, pneumonic infiltration may arise.

Certain peculiarities which are recognizable in the clinical picture in reference to the development of the earliest pulmonary signs and their relation to the bronchial symptoms corroborate this opinion of

Finkler. This will be discussed more fully under the head of diagnosis.

Among the other parts of the respiratory tract which undergo pathologico-anatomical changes, the pleuræ are next to be mentioned. These changes, as clinical experience proves, very frequently follow influenza of the lungs. In mild cases the pathological changes consist of fibrinous flakes, which are in part thin, in part thicker, either circumscribed or diffused. Frequently they may be torn off as membranes, but often the fibrinous masses have become soft and purulent. In a case of marked disease of the pleura together with gangrenous changes in the lungs Pfeiffer observed a purulent coating on the pleura, which upon microscopical examination was seen to contain an enormous number of influenza bacilli, these being gathered together for the most part within the pus cells. In another case of influenza in a phthisical subject, Pfeiffer found the purulent exudate which covered the surface of the lung filled with great numbers of influenza bacilli.

This description does not, however, cover all the cases of empyema complicating influenza. Both Ribbert and Leichtenstern state that the pleural exudations in influenza have a characteristic appearance. The seropurulent exudates are characterized by a thin, cloudy, peculiar dirty yellow appearance of the fluid, which Ribbert designates as "clay-water-like" and Leichtenstern as "cream-of-tartar-like." Ribbert also states that very marked inflammation of the pleura may exist without a previous pneumonia, whether the bronchi at the same time are intact or the seat of inflammatory processes. There can be no question that the observers at the time of the last influenza epidemic were dealing, in those lobar consolidations which involved one lobe or an entire lung, with fibrinous pneumonia which did not differ in any way from ordinary croupous pneumonia. On the other hand, it has been asserted that in such cases certain differences exist. Thus Ribbert found in numerous cases that the cut surface of the hepatized lung was practically smooth, not granular, the exudate soft, rich in cells, but poor in fibrin; and in one case a lobular character could be recognized upon the cut surface of a lobar consolidation, the single lobules not being uniformly altered.

Weichselbaum also informs us that in a series of seven cases he twice found that the diseased lung was not absolutely unaërated, and that its cut surface did not show any marked granulation. In two cases described by Leyden, the cut surface is designated as smooth and not granular, the infiltration as flabby.

Leichtenstern mentions two cases in young, robust individuals in which, despite the short duration of the lobar pneumonia, a grayish-

yellow, soft infiltration was present, such as we are accustomed to see in the later stages of croupous pneumonia. Ribbert points out that such lobar pneumonias are frequently enough combined with lobular pneumonia, in such a manner that in one lung an entire lobe is diseased while the other shows only disseminated areas of consolidation. With respect to the distribution of the process over the entire lung, it has been noticed that the lobular areas vary considerably in extent; at times, areas the size of a hazelnut may be found in one or both lungs, or again the foci run together or approximate one another so closely that there hardly exists any aërated tissue between them. In this manner arise the pseudolobar pneumonias which are often separated in a peculiar manner from the healthy tissue; and thus arise pictures consisting of a peculiar admixture of fibrinous and cellular infiltration which gives to the cut surface a marble-like appearance, in that dense and flabby areas, well marked and indistinctly defined, level and elevated regions, œdematous and hyperæmic, red colored and yellowish or grayish-yellow patches are mixed together irregularly.

Even though these lesions give a remarkable appearance to the lung on account of their various anatomical characteristics, other peculiarities are added as soon as these various areas undergo further development, forming here abscesses, there thickening and contraction. The observation of Koester was peculiar. There existed a diffuse interstitial cellular infiltration, in addition to the plugging of the larger lymphatics with coagulated masses. The alveolar exudate showed, in addition to its poverty in fibrin, a fixed relation between the latter and the cells. The fibrin was found in the centre, spherically arranged, the cells on the other hand between the fibrin and the alveolar wall, so that here an exudation of fibrinous fluid first took place and was followed by an emigration of the cells.

The pathologico-anatomical changes in the circulatory apparatus are far less frequent than those in the respiratory tract. Endocarditis and pericarditis, as well as thrombosis in the cavities of the heart, have been found. The pericardial exudate consists at one time of a cloudy, serous fluid, at another of greenish pus. The coating of the pericardium with fibrin as well as calcification of the same have been observed. Weichselbaum particularly states that in a number of cases the myocardium showed a distinct fatty degeneration. In the larger vessels, especially veins, thrombi which caused a complete obstruction have been observed. Naturally the attention of observers was directed to the spleen, because many clinicians had laid stress upon its uniform swelling. Ribbert observed this enlargement of the spleen relatively seldom; all other observers, however,

have found the spleen distinctly enlarged and mostly of a brown color and an abnormally soft consistence. Leichtenstern also mentions acute fibrinous perisplenitis.

The changes in the intestinal tract have not been frequently discussed. The catarrhal irritation of the stomach and intestines is chiefly mentioned. Only in a few cases were there marked lesions. Jürgensen mentions severe ulceration of the gastric and intestinal mucous membrane, and at the same time the submucosa and in part the muscularis were œdematous and the seat of cellular infiltration just as in the beginning of phlegmonous gastritis. Weichselbaum also described marked disease of the stomach and intestines, and, especially in one case, a very severe inflammation of the mucous membrane of the ileum with hemorrhage.

The liver appeared to partake of the disease but infrequently, so that Weichselbaum speaks of a cloudy swelling in only two cases. Pfuhl, however, describes a more marked change. In one of the cases in which death followed profound changes in the central nervous system, he found the interstitial tissue of the liver more markedly developed than is generally the case, the capillaries well filled, and the liver cells cloudy and granular. In certain parts of the liver lobules he describes the following remarkable changes: 1. Irregular accumulations of small round cells, partly in the centre of the liver lobules, partly in their periphery. 2. In numerous places, likewise in the centre of the liver lobules, there existed peculiar, more or less circular, ofttimes pretty sharply defined structures, which with a low power and on superficial observation gave one the impression of vascular coils similar to those of the kidney. Observed more carefully with a higher power, these were found to consist of a fine net-like tissue whose meshes contained small round cells similar to unstained blood cells. In certain of these structures could be seen a more or less distinct destruction of cellular elements, free nuclei, and detritus. Now and then the reticular structure was present only in certain parts. In these bodies he also found the bacilli which were described by him. Pfuhl is not inclined to place in the group of the so-called lymphomata those round structures in which projections of small round cells run between the neighboring lines of the liver cells, ofttimes up to the intralobular vein. He questions whether these changes in the liver tissue are to be attributed to the bacilli alone, or whether there exists a coagulation necrosis, which is the result of toxic causes. Often icterus of various degrees is found which is to be looked upon as "congestion icterus," caused by a closure of the larger gall passages on account of a catarrhal swelling of the mucous membrane.

In the oral cavity, catarrhal conditions and acute inflammations, as well as ulcerative stomatitis, have been met with. Others have described a sharply defined and at times an intense unilateral redness of the hard palate with displacement of the uvula. The tongue in severe cases is frequently thickly coated. Further is to be mentioned the swelling of the tonsils, which in the gastric cases often gives rise to great difficulty in deglutition, and occasionally inflammation of the parotid gland with fully developed suppuration. The latter has been observed in an intermittent disease.

In the peritoneum hyperæmia is found in some cases, in others inflammation with the formation of a fibrinous coating and cloudy exudate; nevertheless in these cases it is very likely that we are dealing with a peritonitis which existed coincidently with pleurisy.

The kidneys frequently show changes in influenza, which are only of a mild degree, however. Babes describes parenchymatous changes, and Weichselbaum a cloudy swelling. Ribbert found at one time cloudy swelling, at another fatty degeneration of the uriniferous tubules. In the hardened preparations, he observed in the capsules of the glomeruli some coagulated albumin. A very marked case of glomerulonephritis was observed during life by Leyden, and the diagnosis was corroborated post mortem. In this case the gray substance of the kidneys was reddened and already in the first stage of the nephritis, and microscopically presented that appearance which is the most typical form of nephritis following acute infectious diseases, namely, that which is known as scarlatinal nephritis.

The participation of the central nervous system plays a certain rôle in the post-mortem changes, which strikes us all the more because these changes may be very marked and yet not very numerous. Jürgensen describes severe hyperæmia of the membranes of the brain. Kundrat tells us of three cases of cerebrospinal meningitis, of which one was combined with cerebral abscess. Leichtenstern found intense cloudiness and hemorrhages of the pia on the convex surface, and here and there purulent infiltrations in the neighborhood of the veins. At the convex border he observed numerous hemorrhagic, softened, diffuse, greenish-red areas.

Virchow relates a case of lobular pneumonia and mitral endocarditis, in which there existed an apoplectic area in the left hemisphere with numerous smaller hemorrhages in the immediate neighborhood.

Fürbringer reported a similar case. Weichselbaum described a condition in which thick pus was found between the dura and the posterior wall of the right frontal cavity, which was also filled with pus. In one place the dura was swollen, infiltrated with pus, and discolored; the pia was also discolored. In the right frontal lobe

there existed a pus cavity the size of an orange and with hemorrhagic wall, which reached to the anterior part of the brain. The ventricles of the brain also contained pus. Babes mentions a case of purulent basilar meningitis with occasional extension to the convexity. The substance of the brain was œdematous and hyperæmic, the ventricles were filled with a very cloudy fluid.

A. Pfuhl of Cassel has paid particular attention to the severe diseases of the central nervous system which take place in the course of influenza, and has examined pathologically and bacteriologically numerous fatal cases of this disease. In one case he found the veins of the dura mater engorged, and here and there adhesions between the dura and pia, and within these adhesions whitish deposits; in other places he found in the pia mater covering the olfactory nerves and the chiasm of the optic nerve, as well as the under surface of the crus cerebri, glassy, grayish-white deposits, œdema of the brain, and marked dilatation of the ventricles with accumulation of reddish serum. In the same manner the pia mater of the spinal cord showed a venous congestion, posteriorly there were occasional adhesions to the dura mater, and the central part was transformed into a calcareous mass in which the nerve branches were partly embedded; the substance of the spinal cord was greatly softened.

In another case of this group he describes whitish, calcareous masses on the pia mater just at the edge of the great longitudinal fissure, from which white streaks ran in the direction of the cerebral groove; there was exfoliation of the convolutions, the brain substance was moist and anæmic, and abundant serum was found in the lateral ventricles. In a third case he observed filling of the pia with blood, cloudiness of the same, and granulations at the edge of the great longitudinal fissure, with accumulation of fluid and cloudiness in the neighborhood of the optic chiasma, serous exudation in the fossæ of the skull and in the cavities of the brain, especially the large lateral ventricles, and abscesses in the right lobe of the cerebellum. A similar case is mentioned in a work on the epidemic of influenza in the German army, the difference here being that the purulent area was found in the left frontal lobe. These cases of Pfuhl are of special interest because he believes that he found the influenza bacilli in all of them. The bacilli were always found within the blood-vessels. Upon subjecting cut sections of the cerebrum, cerebellum, and spinal cord to microscopical examination he saw in the pia an extraordinary amount of blood, dilatation and at times an increase in the number of the capillaries, as well as in certain places very small exudations into the nervous tissue itself. Furthermore in these places he found a few influenza bacilli in the normal blood-vessels, as

well as in the hemorrhagic foci which were undergoing more or less change. While in the neighborhood of the capillaries and some of the larger vessels there was a great collection of round cells, he found in the central nervous system proper, in the cortex of the brain and the white substance, no particular abnormalities. The cellular elements were especially free from bacteria. In numerous sections of the cerebrum and cerebellum Pfuhl found genuine thromboses; the capillaries of the cerebral cortex were very rich in these, and even with a low power one could recognize the points of obstruction in the section, partly as tortuous, partly as ramifying figures which were stained a deep red. The thrombi were composed either entirely of very small bacilli or of these plus a coccus without a capsule, or finally chiefly of the latter.

Foà of Turin made an examination of the spinal cord in a person who died in the course of an influenza from bronchopneumonia of one lung and hepatization of the other. Here the spinal cord was found entirely filled with blood, its substance studded with small red areas; microscopically numerous hemorrhagic foci were found in all parts of the spinal cord, particularly in the upper two-thirds, and in the upper third of the cervical portion. In some places degenerative changes could be seen, the eighth nerve was enlarged from five to six times its normal size, and the nerve fibres were degenerated. The hemorrhagic areas were situated especially in the posterior horns almost always at the periphery, the degenerated areas for the most part in the lateral horns. The gray substance and the posterior horns were not in the least altered. In eleven post-mortem examinations, Hetweg found as a constant symptom a very marked hyperæmia of the entire central nervous system, such as we otherwise never meet with. The arteries at the base of the skull were particularly engorged with blood, and the consistence of the cerebrospinal axis was always increased. For that reason Hetweg speaks of an influenza hyperæmia and considers this, not an ordinary vasomotor one, but a process which is the forerunner of an inflammation.

Symptomatology.

Influenza is one of the infectious diseases which causes marked functional disturbances in all parts of the body, so that in reality no organ is found entirely normal. Inasmuch as the individual symptoms appeared with varying intensity, clinicians were from the very beginning inclined to the belief that the seat of the infectious agent was distributed over the entire body. During the last widespread epidemic this opinion had taken hold of physicians to such a degree

that one was really greatly surprised to find post mortem all the organs so very little and so very irregularly the seat of pathological changes. The investigations of pathologists have not yet placed us in a position to determine with any certainty to what extent, in an infectious disease, the resulting changes take place at the primary seat of the disease, and to what extent the entire body, at the same time or at a later period, shows symptoms of disease due to changes dependent upon poisoning by toxins. In the case of cholera we know positively that the bacillus finds its point of attachment in the intestines, that an enormous increase takes place on the superficial surface of the intestines, and that the symptoms of cholera, which are the most severe that we can see in the human being, are caused by the absorption of toxic substances formed in the intestines.

Until within recent date we were loth to acknowledge that the minute amounts of toxic substances elaborated by the bacteria could give rise to marked general symptoms. Upon this subject our knowledge has also become very much clearer. We know, for example, how tuberculin in a very dilute condition produces severe effects upon the organism. We know, on the other hand, that antitoxin, for example that of diphtheria, suffices in small amount to produce specific and remarkably far-reaching functional changes in the human organism. For that reason it is now held that in an infectious disease there need not be any general distribution of the bacilli in order to produce severe general symptoms. In influenza above all this stands out prominently.

General Symptoms.

There exists a typical form of influenza which is caused by the influenza bacilli alone, and which runs its course without complication of other bacterial infection. In this form it frequently becomes evident that there are extraordinarily few symptoms referable to the part first invaded, but that on the other hand the general symptoms dominate. In people apparently in perfect health there suddenly appears a marked general discomfort—severe headache, chiefly in the frontal region, muscular pains which very frequently exist in the loin but also in the muscles of the extremities, and in addition often marked weakness. In the midst of these symptoms the temperature of the body is suddenly elevated, sometimes with one chill, more frequently, however, with repeated chilly sensations. There are very mild cases in which nothing further appears. The picture becomes somewhat severer when a marked redness of the face and a feeling of intense heat develop; the eyes, on account of hyperæmia of the conjunctiva, appear reddened and the sclera assume a slightly yel-

lowish, icteric hue. In individual cases this icteric color spreads itself over the skin and may there become intense. There is usually a catarrh of the upper air passages in addition to coryza, or a severe catarrh of the mouth, with thickly coated tongue, and hyperæmia and swelling of the pharyngeal mucous membrane. The involvement of the neighboring nasal cavities is evidenced by pain in the frontal sinuses. Frequently the larynx is prominently involved from the very beginning, so that hoarseness or aphonia constitutes a more prominent symptom than pain; here also the mucous membrane shows marked redness and swelling.

In the pharynx the swelling may reach such an extent that we are reminded of a beginning diphtheria, the tonsils stand out prominently, and the uvula is displaced. Now and then a distinct follicular inflammation of the tonsils arises, sometimes we see very superficial mucopurulent spots and lines on the reddened palate, tonsils, and rest of the pharynx, and occasionally there is seen a very sharply defined punctate redness.

Inasmuch as we are accustomed to find the spleen swollen in acute infectious diseases in which infection occurs through the blood, the attention of physicians was early turned in this direction, and as a matter of fact it was found that there is often a swelling of the spleen at the beginning of influenza. In individual cases the spleen becomes distinctly palpable, and we can follow the course of the enlargement with the onset of influenza and its disappearance again upon the decline of the disease.

Prompted by the appearance of icteric symptoms, which he found in eighty-eight per cent. of his cases, Bäumler directed his attention to this perhaps valuable diagnostic symptom. He could not, however, demonstrate the presence of bile pigments in the urine, and yet in some cases he obtained a distinct urobilin reaction, not quite so marked, however, as would be expected in actual jaundice. Hayem states, on the contrary, that urobilinuria is constantly found in influenza. Senator obtained the diazo reaction in numerous cases and found a large amount of indigo in the urine. It is worthy of note that the above-mentioned yellow color of the sclera appears in this infectious disease, since we also see it in other forms of septic changes, in poisoning, and in cases of internal hemorrhage. The examination of the blood showed that not only is there marked diminution of hæmoglobin, but also a destruction of numerous red blood cells takes place during the course of influenza, as Schermer and Přibram proved. We find also, as a rule, a strikingly large number of degenerated red blood cells.

All these symptoms of influenza disappear in a short space of

time, so that few regard the individual attack as a pyrexia with all the symptoms that belong to a fever. As far as the body temperature itself is concerned, we find that this (very frequently directly after the chill) rises to 40° C. (104° F.) and over; indeed the temperature at the beginning of the attack is usually the highest seen in mild cases. This sharp rise is not always present, but frequently a somewhat more gradual development of the temperature is observed, sometimes as a matter of fact the fever rises in such a manner that the acme is reached only on the second or third day. Often this attack of fever is remarkably short so that in a few hours the normal temperature is once more reached; but we can hardly expect that the other symptoms should also disappear in the same short space of time. The latter more frequently exists for a number of days after the fever, and proves thereby that the severe subjective symptoms are not to be attributed to the elevation of temperature alone. In other cases the fever lasts a much longer time, sometimes a number of days. In these cases of continued fever, despite frequently repeated examinations, we are often surprised to find no other or only very slight symptoms of organic trouble appear. Upon closer examination of the lungs, we often find in numerous small areas crepitant râles, which, however, are only heard upon listening very attentively. During the recent pandemic of influenza I always from the first looked for such pulmonary symptoms, and found them very frequently. The favorite seat for this sign seems to be at the border of the lung above the liver or in the lingula. Slight as such symptom may be, still it is of very great importance for the diagnosis of the disease and in support of the belief that the cause of the influenza found entrance through the substance of the lung itself, in those cases in which the upper respiratory passages remain free and yet marked general symptoms have arisen. Though the fever remains for a number of days it does not follow a fixed type. It is just as common to see a frank continued fever curve as one with remissions and exacerbations. Even for these case no rule can be laid down. There are intermittent as well as remittent temperature curves, but these are so irregular that the reversed type (morning elevations and evening remissions) is occasionally seen. Very marked elevations of temperature up to 41° C. (105.8° F.), or hyperpyrexia, are occasionally observed in an ordinary attack of influenza, but they make the existence of a complication very probable. They have been observed especially in patients in whom severe cerebral symptoms, such as unconsciousness, coma, and hemiplegia developed, and who for the most part died. According to the observations of Leichtenstern and Teissier, a very frequent, in fact a pathognomonic symptom of the

disease is the fall of the temperature for one or two days while the remaining symptoms continue, this being followed by an exacerbation with aggravation of all the symptoms, so that days of normal temperature alternate with those upon which fever exists. This has been designated polyleptic influenza. Leichtenstern reported a very interesting case in a child nine months of age, in which severe complications arose, the temperature reached 41.3° C. (106.3° F.), and yet the course of the disease was a mild one. In the German army reports a case is mentioned in which the temperature was 41.5° C. (106.7° F.), and five minutes after death reached 43° C. (109.6° F.).

In rare cases it has happened that during the protracted course of a complicated influenza, the temperature has assumed a regular quotidian intermittent type, with euphoria in the fever-free period, the fall of temperature being accompanied by sweating, so that the picture of a malaria is presented. Cases have also been described in which influenza began in a typical manner and the temperature remained continuously for two to three weeks at 39°–40° C. (102.2°–104° F.) without any respiratory or other complicating symptoms, so that the possibility of typhoid fever was thought of. All the foregoing may be observed in entirely uncomplicated cases.

As regards the skin, the severe redness and swelling are evident as a rule even in ordinary attacks of influenza, and the face may assume a puffy appearance. In this case there must exist a vasomotor paralysis of the cutaneous vessels. The redness of the skin is not always uniform, but appears frequently in the form of an exanthem resembling that of measles or scarlet fever, which is especially marked on the face, the forehead, the chest, and the buttocks, less frequently on the upper, and least frequently on the lower extremities. On the face, a widely diffused punctate redness frequently appears and once in a while an urticaria.

The pulse in influenza is a peculiar one. The frequency increases with the elevation of temperature but is as a rule unduly great, so that there is a disproportion between the temperature and the frequency of the pulse. The pulse as a rule is soft and easily compressible and is rather indicative of a cardiac weakness.

Certain other symptoms have been observed in special cases of influenza; for example, an attack of syncope suddenly develops, or marked evidence of trouble in the nerve centres, such as vertigo and unconsciousness, appears, so that the symptoms may remind one of an apoplexy. In the garrison hospital of Munich the peculiar observation was made in 127 cases that after the temperature had begun to fall a slowing of the pulse even to 54 or 56 occurred. This bradycardia was combined with a small pulse, and strange to say in the majority

of cases was more evident in the evening than in the morning; at the same time the temperature assumed the inverse type—for example, evenings 36.8° (98.3° F.), mornings 37.2° (99° F.). This slowing of the pulse is said to be constant during convalescence, and lasts as a rule from five to eight days, in some cases, however, ten days to three weeks.

As further proof of the fact that the poison of influenza really affects the myocardium or its nerve supply, might be mentioned the studies of Anton in the medical clinic of Würzburg. Here in a number of cases there existed blowing systolic murmurs, especially at the apex, but they were also audible over the other large vessels. At the same time the second pulmonary sound was not accentuated, and in seven per cent. of the cases the area of cardiac dulness was not altered. For the most part the murmurs disappeared on the second day without leaving any permanent changes. That it was not the fever which gave rise to these murmurs is evident from the fact that this condition was found precisely in those patients who had but little rise of temperature, whereas in many patients with high fever no murmurs developed. Therefore we must seek for the cause of this in a direct action upon the muscular structure or ganglia of the heart, which leads to a defective contraction of the organ, especially of the papillary muscles, and thus to the formation of murmurs. This corresponds to our experience in other infectious diseases. The action of the influenza poison upon the heart is very noticeable in those who already have an affection of the heart and in old people. In these cases there occurs very frequently an irregularity of the heart's action, an irregularity which is considered by many observers, for example Drasche, as a very suspicious symptom. Not only does the pulse become irregular but at the same time unequal, and this together with coldness of the extremities, restlessness, and anxiety points to a very marked cardic weakness.

Some authors call our attention to the fact that for a short space of time during the course of influenza the pulse may assume a very alarming character as regards its rapidity and smallness. Huchard, who recognizes a peculiar form of cardiac grippe which is characterized by syncope, slowing of the pulse, attacks of irregular or intermittent heart action, and now and then by attacks of pain such as are seen in angina pectoris, describes as a special symptom the increase of the pulse beat from 80 to 120–130 when the patient sits up. As soon as the patient once more assumes the horizontal position the pulse returns to its original rhythm; Huchard looks upon this as a sign of a commencing myocarditis and calls it *pouls instable.*

Symptoms Referable to Individual Organs.

The previously depicted symptoms may be looked upon as general symptoms of the disease; they have something characteristic about them and are more or less marked in an attack of influenza. However, the picture of influenza may assume a manifold character, depending upon whether one or another organ shows particular functional disturbances. This was noted in the earlier as well as in recent epidemics, and from the earliest time pains have been taken to classify these symptoms in certain groups in the belief that they indicate that influenza had settled chiefly in one or the other organ.

In consequence of this it has been made possible to classify influenza in various ways. There can be no doubt that such a classification proves advantageous as regards statistics and for the rapid characterization of a disease; but a real developed classification in which the individual sections are constantly found and sharply distinguished from one another, would be idle and, in the light of our present idea of the nature of influenza infection, also false. In 1837 Ebel arranged a somewhat complicated classification, as follows:

A. Influenza of the mucous membrane of the respiratory organs: (1) Influenza catarrhalis simplex; (2) influenza catarrhalis nervosa sive gravior; (3) influenza trachealis et bronchialis; (4) influenza pleuritica.

B. Influenza of the mucous membrane of the digestive organs: (1) Influenza anginosa; (2) influenza gastrica sive abdominalis.

Ebel distinguishes three stages of the disease, namely: (*a*) Stadium congestivum sive siccum; (*b*) stadium serosum sive catarrhale; (*c*) stadium mucosum.

We do not see here much reference to any particularly striking participation of the nervous system. This appeared more prominently in the classification which Haeser attempted in 1834. He distinguished a stadium vegetativum, a stadium animale, and a stadium sensitivium, in addition to an influenza encephalitica and cholerica. Lange in 1837 distinguished an inflammatory-catarrhal and a nervous-gastric form. Taking the cases observed in the epidemic of 1889 and 1890 as a basis, Huchard formulated the following classification: (1) Bronchopulmonary influenza; (2) cardiac influenza; (3) gastric and intestinal influenza. Strümpell recognizes four forms: (1) A typical form; (2) a catarrhal form with special involvement of the respiratory apparatus; (3) a catarrhal form with special involvement of the digestive apparatus; (4) a rheumatic form. Leyden divides influenza into gastric, catarrhal, and nervous forms.

We learn from the collective report upon the influenza epidemic of 1889 and 1890, which Hiller arranged, that the majority of physicians in recent times recognize three forms, viz., the nervous, the respiratory, and the gastric, while some add as a fourth form the rheumatic. It is interesting to see that these various forms of influenza in the course of an ordinary epidemic do not commonly appear at the same time but successively and usually in fairly regular order. In most places the nervous form preceded, and indeed commonly the purely nervous form, that is, one which is characterized by general symptoms such as a bruised feeling, depression of spirits. This was followed frequently by marked local nervous symptoms, hyperæsthesias, neuralgias, and paralyses; later, the respiratory and the gastric forms were added. In other places the succession was just the reverse. The first cases of the epidemic presented prëeminently gastric symptoms, such as colic, vomiting, diarrhœa, and only with the further development of the epidemic respiratory and nervous symptoms came to the front. The predominance of one or another of the various forms in special places has been described as very remarkable. Thus Dr. Salm in Völklingen near Saarbrücken observed that in one village the gastric symptoms appeared most prominent, in another the nervous symptoms predominated, in a third practically only catarrhal symptoms were seen. Dr. Lebahu in Halchow in Mecklenburg informs us that the picture varied in the different communities. In one place cough and coryza prevailed, in another diarrhœa, in a third only nervous symptoms. Even in single houses the epidemic showed a peculiar character. Dr. Vossen in Düsseldorf found that in some houses sometimes the nervous, sometimes the respiratory, sometimes the gastric form prevailed in all the patients. Some observers have endeavored specially to subdivide some of these forms; thus Stiller recognizes a catarrhal, a gastrointestinal, and a nervous form, but he sharply subdivides the latter into a neuralgic and an adynamic form and adds the pneumonic as a particular form. Others have particularly emphasized the fact that the numerous forms frequently appear in one and the same patient. Thus Robertson and Elkins compiled the statistics of 140 cases of influenza in the Royal Asylum at Edinburgh, and of these the nervous system was attacked in 97.1 per cent., the respiratory tract in 77.1 per cent., the digestive system in 55.7 per cent.

The Upper Air Passages.

It has already been mentioned in the section on General Symptoms that the conjunctiva and the mucous membrane of the nose and pharynx are often the seat, in cases of simple influenza, of easily

recognizable changes. As to the mucous membrane of the respiratory tract proper, from the larynx downwards to the lungs, we find that there is a special proneness to catarrhal inflammation of this part in influenza. These catarrhal changes are frequently localized, involving the mucous membrane of the larynx alone or only that of the bronchioles, but equally often we find the catarrh extending throughout the entire tract by continuity, from whatever point it started.

During the last great epidemic of influenza the involvement of the *larynx* was exceedingly irregular in the frequency of its occurrence. Many physicians described this complication as singularly rare. Thus B. Fränkel in 638 cases of throat trouble, treated at the University Clinic from December 5th, 1889, to February 20th, 1890, saw only 45 due to influenza. Lazarus states that, except for a slight reddening of the mucous membrane, involvement of the larynx is a very rare occurrence in the course of influenza. Other observers, on the other hand, noted a special frequency of grippal laryngitis. Schulz, for example, found 66 per cent. of his cases to be catarrhal influenza and of these 16 per cent. were put down as laryngitis. Luntz regarded laryngeal trouble as the most frequent of the symptoms of influenza, and Paul Hoch even held the opinion that the mucous membrane of the larynx and upper air passages was the special seat of the influenza infection. This striking variation in the frequency with which laryngeal implication was noted by different observers was due sometimes to external causes. It can be readily understood that sufferers from influenza, in whom the head pains were the most prominent symptoms or in whom the general manifestations of the disease were so severe as to overshadow in great measure the laryngeal complication, would not be found usually in a dispensary for throat diseases or in the consulting-room of a laryngologist. General practitioners are for the most part, during the height of an epidemic of influenza, much too busy to concern themselves especially with the extent to which the larynx is invaded by the disease. In the presence of the severe cough and general malaise at the beginning of an attack of influenza, the family physician does not usually regard a special examination of the larynx as necessary or of much importance. The only conclusion which we can formulate, therefore, is that the implication of the larynx in influenza is seldom of very great intensity.

We have to distinguish clinically between pure hyperæmia of the larynx and swelling or infiltration of the tissues. With the hyperæmia belongs the hemorrhagic form of laryngitis which is among the most frequent of the affections of the larynx. Löwenstein, Leyden, and Leichtenstern referred as early as 1890 to cases of hemorrhage

from the larynx, and Fränkel observed in all cases a redness of the mucous membrane, which in two cases went on to actual laryngitis hæmorrhagica. It will, I think, be practically useful to quote a few observations from the report of Lazarus, of Berlin, for they will show us how the laryngologists themselves regard affection of the larynx in influenza. Loblinsky describes the redness of the laryngeal mucous membrane as being more intense than he has ever seen it in simple acute laryngitis. Marano had among his cases three of hemorrhagic laryngitis, and observed in every instance an intense redness of the arytenoids, the epiglottis, and the vocal cords, in general a very marked injection of the vessels, and not seldom a resultant bloody expectoration. Rathgen had a similar experience. But here also we find strikingly contradictory reports, for Landgraf and Krakauer do not mention a single instance of such hemorrhages in spite of the abundance of their material.

The swelling of the mucous membrane in some of the reported cases involved the entire larynx, in others it was more circumscribed. Lazarus inclines to the opinion that the first form is more common than would be inferred from the reports in which it is specifically mentioned; he believes that the sore throat and also the hoarseness so frequently mentioned in reports of cases are due to swelling of the laryngeal mucous membrane. In all of his cases Fränkel found a marked swelling of the mucous membrane; he says that this sometimes presents a picture such as that described first by Rauchfuss as pseudo-croup, in which inspection shows three folds: first, the false vocal cords, then the vocal cords, and beneath these chiefly anteriorly a subglottic swelling which looks like another mucous membrane fold. Schaefer has described a very marked swelling of the arytenoid folds and of the false vocal cords so that the first are entirely hidden from view.

Landgraf has described especially the circumscribed swellings of individual parts, and he reports one case in particular in which the interarytenoid region was the seat of a peculiar form of inflammation. This circumscribed affection was the primary one and had given rise to a consecutive œdema of the glottis which threatened the life of the patient. Lazarus regards as belonging to this class the cases reported by Moure and Gurcan. Herzog describes the swelling in the interarytenoid space as laryngitis postica. This may lead to circumscribed or diffuse laryngeal or glottic œdema threatening life. Especially noteworthy are the published reports of B. Fränkel, who found that the middle portions of the vocal cords, which were in general reddened, were of a dirty white color. He regarded this as characteristic of a fibrinous infiltration of the cords, which might be

of value as pointing to a diagnosis of influenza. As also peculiarly characteristic he mentions a crust formation localized especially in the subglottic region and the posterior wall of the larynx.

Le Noir has described the occurrence of ulceration affecting chiefly the anterior half of both vocal cords, of superficial nature and healing with the disappearance of the influenza.

When the infiltration is found in the deeper portions of the mucous membrane it invades also the muscular tissues, in consequence of which arise paralyses and motor disturbances in the larynx. Indeed Lazarus says that there is a form of the disease in which the primary seat is in the muscular and submucous tissues causing marked motor disturbances, while on the mucous membrane only slight evidences of catarrhal lesions are to be seen. It is very probable that the frequently long-continued, possibly even permanent aphonia, or at least impaired voice formation, may be referable to a lesion of this character. As a result of a very thorough study of the literature of this subject Lazarus comes to the conclusion that a characteristic laryngeal symptom of influenza is an otherwise seldom observed hyperæmia and infiltration specially localized in the posterior portion of the organ. Many of the paralytic symptoms are undoubtedly of a nervous origin and are not directly dependent upon the local lesions. The course of this affection of the larynx points also very clearly to the fact that, in most cases at least, the process is a deep-seated one; recovery is extraordinarily protracted, and the sequelæ are often of a kind resembling closely those of diphtheria, that is to say, local sequelæ of a severe general disease.

A case reported by Leichtenstern is especially noteworthy in this connection. It was one of a strong nineteen-year-old girl who was seized, on the third day of a mild influenza, with a very severe and acute œdema of the glottis, necessitating an immediate tracheotomy. This patient had neither coryza nor tracheitis and bronchitis, and the larynx alone was the seat of a severe inflammation. The laryngeal abscess opened a few days after the tracheotomy and discharged a large quantity of pus. This was an example of what Leichtenstern has called acute phlegmonous grippal laryngitis.

The affection of the *trachea* often accompanies that of the bronchi and larynx, but sometimes it occurs alone and is especially marked. We have met with many cases in which in the midst of marked general symptoms of influenza a very severe cough was present, while the most careful examination of the larynx, bronchi, and lungs failed to furnish any explanation for its occurrence. Inspection with the laryngoscopic mirror in these cases revealed a diffuse redness of the mucous membrane of the trachea, but nothing else. In proportion

to the meagreness of the results of this examination, however, is the severity of the initiative symptoms on the part of the trachea. Even more than in the case of catarrhal affections of the larynx is cough a prominent symptom of tracheal influenza, and indeed it often resembles pertussis, especially in the fact that but little explanation for the cough is to be found in the alteration in the air passages; pain along the course of the trachea is also often complained of. In consequence of the marked tenderness of the trachea in these catarrhal affections, pressure in this region often causes pain or excites cough.

Usually, however, the tracheitits occurs in conjunction with the influenza bronchitis, but even when this is the case many authors unite in believing that the cause of the strong fits of coughing is seated chiefly in the trachea, especially at its bifurcation and in the primary bronchial trunks. The attacks of cough are often of exceeding severity and distress the patient night and day. Even in the earliest recorded epidemics special mention is made of the spasmodic character of the influenza cough. Leichtenstern relates in his work on Influenza that Short, writing in 1510, described the frightfully distressing cough and the consequent danger of suffocation. He also states that the term *coqueluche* was first, in 1510, used to designate influenza and was only later applied to whooping-cough, and that in 1580 influenza was called *Schafhusten*, which term also is now employed to designate whooping-cough. Still earlier, in 1410, Pasquier attributed to the severe cough the hemorrhages and the frequently observed abortions of pregnant women. The cough accompanying tracheitis is often quite dry throughout the entire course of the disease, and it was on that account that during the latest influenza epidemic there were so many reports of coincident epidemics of pertussis. The following figures give us an idea of the frequency of catarrhal tracheitis in influenza: Schulz states that it occurred in 53 per cent. of the cases in Hamburg, Krehl in 82 per cent. in Leipsic, Stintzing in 57 per cent. in Munich, and Anton in 59 per cent. in Würzburg.

The most frequent of all the localizations of influenza is that in the *bronchi.* In ordinary bronchitis *a frigore* we are accustomed to find the entire bronchial system involved in the catarrhal process, but in influenza we note with special frequency a partial implication only of the bronchial tubes. In the beginning the bronchial mucous membrane is simply hyperæmic. While the fever is rising and the attack of influenza is beginning there is frequently scarcely any evidence of secretion to be detected on careful examination. At other times, very early in the course of the affection, we find the physical signs of a

swelling of the bronchial mucous membrane, as shown by a heightened respiratory murmur at certain points or by a loud inspiratory sound. We often remark that the inspiratory murmur at a certain point is at first very faint and then suddenly becomes very loud. Frequently, however, even at an early stage we find severe cough and short breathing amounting at times to actual dyspnœa.

Doubtless many peculiarities noted in the physical examination of the chest are due to the presence of the bronchial disease. Thus we find localized spots of atelectasis, slight dulness on percussion, and weakened respiratory murmur. It is seldom that this dry catarrh lasts for any great length of time, and usually a secretion from the mucous membrane occurs early, and we then find the physical signs of bronchial catarrh together with an expectoration which is usually purulent from the outset. The sputa are often from the very beginning of an intense yellow color, sometimes of a more greenish-yellow appearance. It seems to me doubtful whether the bloody stain, which is often seen in the sputum and which gives it a very peculiar flesh-colored tint, is due to the bronchial inflammation alone or whether it does not indicate that the pulmonary tissue is already involved.

While, as we have said, the dry catarrh may persist for quite a period, there are other cases in which the secretion increases progressively until it ends in an actual bronchorrhœa, the expectoration amounting to as much as a litre in the course of a day. Examination of the chest shows then an exceeding variety in the character of the râles so that almost every form of rhonchus may be heard. The sputa sometimes become nummular in shape. In the course of such an inflammation bronchial dilatation may occur early, and it would seem even as though this profound anatomical change might take place without any participation of the pulmonary tissue. This alteration may persist for quite a period and may even pass into a deep-seated chronic affection having a most injurious influence upon both circulation and nutrition. A bronchial dilatation may sometimes be produced at isolated points. In such cases we find that for a long period there is an expectoration of sputum of a special appearance, perhaps once every day, after the discharge of which for a time there is no further expectoration until the sputum had again collected so as to fill the dilatation in the bronchi. One notable symptom is the coughing up of fibrinous casts of the bronchi, which is not of frequent occurrence, yet is sometimes noted.

Grippal bronchitis is such an important and such a frequent manifestation of the disease that I think it will be useful to report a few cases. In all these cases the Pfeiffer bacillus was found, so that

there could be no question but that the affection was really a primary bronchial influenza.

A locksmith, 61 years old, was suddenly seized, three days before being seen, with a chill, headache, cough, expectoration, pains in the limbs, and a feeling of exhaustion. His face was markedly cyanotic, breathing was difficult, but there was no pain in the chest. There was dulness on percussion in the lower part of the right side of the chest and the breathing here was rough. All sorts of bronchial râles were heard over the entire lung. The pulse was small and frequent. Nine days later the subjective symptoms were less marked. The cough persisted and there was profuse expectoration. There was no longer dulness on percussion, but the whistling and bubbling râles were still audible over the whole lung. Ten days later the cough, expectoration, and râles were still present, but less marked. At the end of another ten days the patient was discharged. The fever, which lasted only a few days, varied from about normal to 39.4° C. (103° F.). On the first days after the patient's admission the expectoration was scanty, exceedingly ropy, and purulent. It contained large masses of influenza bacilli so that in some parts absolutely nothing else could be seen; here and there was a diplococcus, but there were no streptococci. At the end of the first week, as the dulness on percussion disappeared and the expectoration increased in amount, the latter contained only influenza bacilli. The patient's general condition improved rapidly, but even on the day of his departure from the hospital the sputa still contained specific bacilli.

A laborer, 72 years of age, had complained for two weeks before admission to hospital of anorexia, malaise, and a dragging sensation in the back. He had had a cough with expectoration for a long time. There had been no chill. The temperature was 38.6° C. (101.5° F.), the pulse and respiration were rapid. The percussion note was clear in the upper part of both lungs anteriorly, slightly dull over the lower portion of the left lung anteriorly, and distinctly dull over the right lower lobe posteriorly. The breathing was roughened in the upper part of the thorax anteriorly, and posteriorly in the right lower lobe there was pneumonic respiration with moist râles at the upper limit of dulness in this region. There was fine crepitation over the lower part of the left lung posteriorly. A bacterioscopic examination showed only diplococci in the sputa. On the fourth day the dulness was less pronounced over the right lower lobe and there were more moist râles; in the left lower lobe there was diminished resonance in the middle portion passing into flatness below, where were heard pneumonic respiration and râles. A week later the dulness in the left lower lobe had entirely disappeared. Moist râles were audible. In the right middle lobe there was a spot of dulness with pneumonic breathing. The expectoration was purulent and contained now both diplococci and influenza bacilli. Two weeks later there were few influenza bacilli to be found, but there were many streptococci. The patient was discharged at the end of another three weeks. The fever lasted only about a week and was never as high afterwards as it was on the day of admission. This case was

one of chronic bronchitis followed by bronchopneumonia. It is questionable whether the first pneumonic foci were occasioned by the action of influenza bacilli; at all events these were not found in the sputum at this time. But coincidently with the formation of a patch of pneumonia in the right middle lobe the sputa became purulent and contained influenza bacilli. This condition lasted about twelve days, then the influenza bacilli became less numerous and streptococci appeared in greater numbers. This stage lasted about three weeks, after which the bronchitis also subsided, and the man was discharged entirely cured.

A roofer, 25 years old, had complained for a week before admission of sore throat, hoarseness, cough with expectoration, malaise, and weakness. There was slight bronchial breathing. The tracheal mucous membrane was very red and both vocal cords were swollen and reddened. During the week following admission the temperature varied from slightly below normal to 38.4° C. (101.1° F.). The sputum was mucopurulent in character and contained purulent plugs which were sometimes in the form of complete casts of the capillary bronchial tubes. These contained influenza bacilli exclusively. At the end of a week a marked improvement in the symptoms took place, and at the end of a fortnight examination of the sputa showed the presence of many other bacteria and of only a few influenza bacilli; the improvement was progressive.

These few examples show us the typical course of bronchitic influenza as we have observed it in very many cases from 1889 to the present time. They are all alike, and there seems to be as yet no diminution in the severity of type. Especially noteworthy is the fact that the bronchial secretion soon becomes purulent in the presence of influenza bacilli, so that the rapidly occurring purulence of the expectoration in a case of acutely progressive bronchitis offers strong presumptive evidence that there is an influenza infection. The diagnosis is, however, not so easy, for we often observe a similar condition of the sputa and general symptoms of the same nature in cases of streptococcus infection. I am never certain of my diagnosis unless I have been able to determine the presence of the influenza bacilli or of streptococci.

This mode of action of what bacterioscopic examination shows us to be pure influenza bronchitis confirms what we have remarked concerning the acute form of this disease during the present great epidemic, viz., that isolated cases occurring at other times act much in the same way as the mass of cases during an epidemic. Very often the severe poisoning of the body gives rise to marked symptoms on the part of the nervous system or of the digestive organs even when the local process in the bronchi is of limited extent. The following point is of special importance as an aid to exact observation. The influenza bacilli may remain in the bronchial tubes beyond the

time of the disease, far longer indeed than is usually imagined. In this connection it is to be noted that influenza occurs with special frequency in cases of bronchitis having a different etiology. We often see patients who have had for a long time a cough due to an ordinary bronchial catarrh, subsequently acquire an influenza. Usually this is regarded simply as an exaggeration of the already existing bronchitis. I saw, for example, a patient with extensive chronic bronchitis, the examination of whose sputa showed the presence merely of staphylococci and streptococci. A week later examination of the chest revealed dulness in the upper lobe of the right lung posteriorly, and on the same day the presence of influenza in the sputa was noticed for the first time. The symptoms gradually disappeared, but the influenza bacilli could still be detected at the end of four weeks. In the absence of this bacterioscopic examination one would never have imagined that there was a new and different infection; it would merely have been supposed that this was an instance of what is thought to be an ordinary occurrence in the course of chronic bronchitis, namely, the appearance from time to time of a bronchopneumonia.

While now we have on the one hand an explanation of these cases of increased severity of symptoms, we see also on the other hand how such chronic patients may act as special sources of infection, carrying the disease to the well and to other invalids, especially those suffering from phthisis or bronchitis. We are all accustomed to see many of our old bronchial cases return to the hospital as permanent boarders during the inclement season of the year, their sufferings being increased at such times. In many of these cases the increase in the symptoms is undoubtedly due to an influenza infection, and, what is of special importance as regards the matter of spread of the disease, the typical symptoms of influenza are wanting in these cases. Whether this is due to the fact that the patients have already harbored the influenza bacilli for a long time or whether the symptoms are modified through the presence of the older infection, I will not attempt to decide. It is of great importance to remember that in these cases the influenza bacilli may disappear for a time from the sputa and appear again later. We might perhaps designate these as cases of intermittent influenza.

By reason of the importance of this fact in its bearing upon our knowledge of the mode of infection and spread of influenza, I think it of service to report the following case:

We treated in the hospital from September 26th, 1893, to October 16th, 1894, the date of his death, a patient with chronic bronchitis. He had suffered from slight dyspnœa for a year, but was led to

seek admission to hospital on account of an increase in this and also on account of scurvy-like symptoms in the mouth and on the skin. The pulse was 70, respirations 44. The thorax was barrel-shaped. There was dulness on percussion posteriorly at the level of the ninth rib on the left side, and resonance above this point was not clear. On the right side the liver dulness extended up to the seventh rib in the mammillary line. The area of heart dulness was much reduced. Bronchial râles were heard over the entire left lung, and crepitation over the area of dulness on percussion. The gums were swollen but not bleeding. The teeth were loose. There were purpuric spots on both upper and lower extremities, but especially on the upper arms and thighs. No tubercle bacilli were present in the sputum. Every morning he suffered from an eruption of urticarial wheals on the hands, forearms, and legs. A month after admission the patient complained of increased dyspnœa, and the bronchial râles were louder and more numerous; the expectoration increased, the appetite failed, and the patient could not sleep. The emphysematous and bronchitic symptoms continued with varying degrees of severity, but the patient was able to be out of bed all day. There was a bronchial dilatation posteriorly on the left side between the seventh and ninth ribs. Areas of dulness appeared from time to time over the left lung posteriorly, but these usually cleared up quite promptly. The frequently repeated examinations of the sputa had, up to January 20th, 1874, shown constantly the presence of diplococci and streptococci, but on this day influenza bacilli also were found, and at the same time there was a marked deterioration in the patient's condition. There was no change in temperature, which showed the usual streptococcus curve, but the patient suffered from extreme weakness, the pulse became very bad, and the dyspnœa was pronounced even when perfect rest was maintained. An improvement soon occurred and the influenza bacilli disappeared from the sputa at the end of ten days. The bronchiectasis persisted and was the cause of a profuse purulent expectoration. The apparent cavity was so large, indeed, that there was question for a time of operating upon it. I have so often, however, observed symptoms of this character in cases of bronchiectasis in which no cavity of any size existed (I have even seen an incision made in the lung without the discovery of any cavity), that I am now opposed to operative interference in such cases. We therefore resorted to antiseptic methods, but with very indifferent success. In the night from the 14th to the 15th of February, the patient was seized with a diarrhœa, having eleven passages between midnight and daybreak, and felt greatly prostrated in consequence. The diarrhœa was, however, checked by means of appropriate remedies. On the 25th of this month the patient was out of bed for a short time and sat by the window. The following night he had fever and a hard chill. Following that the man was constantly in bed, and suffered much from difficulty in breathing. At this time the sputum was found to contain a large number of influenza bacilli. In April streptococci appeared in great numbers but the influenza bacilli still remained. The patient died of exhaustion in October, and at the autopsy many bronchial dilatations

were found, in the contents of which streptococci and influenza bacilli swarmed.

During this illness I tried a long list of remedies to which antiseptic properties are commonly attributed, such as creosote, guaiacol, terpin hydrate, carbolic acid, quinine, etc., but no benefit followed the internal administration of any of them. Inhalations of lime water with carbolic acid, camphor, peppermint oil, and even of chloride of lime solutions, were tried, but without effect upon the number of bacteria in the sputum.

This case shows with what persistence the bacteria remain in the sputum, and how especially the influenza bacilli may swarm in the purulent bronchial secretion despite all our antiseptic measures. The influenza symptoms were often absent for long periods, and there were alternating periods of improvement and deterioration occurring in such a way that, without the evidence of the bacterioscopic examination, no one would have imagined that we had to deal with such a chronic influenza. I need not dwell more particularly upon the menace which such a person might be to the health of those about him.

Beck's cases are of special value because he has worked up in a most excellent manner the relation existing between the diseases and the presence of Pfeiffer's bacillus. He also writes that during the epidemic of influenza he observed a large number of cases in which the patients, a few days after the beginning of their illness, were found to have diffuse bronchial râles over one or both lungs. In these cases the sputum swarmed with great numbers of influenza bacilli so that Beck diagnosed them as cases of bronchitis directly due to influenza, or at least to the presence of influenza bacilli.

Bronchopneumonia.

Our knowledge of grippal bronchopneumonia, which must be regarded as a specific affection due to the action of the influenza bacillus, has been greatly increased by the reports of Beck from the Institut für Infektionskrankheiten. The cases there observed were quite uniformly of such a benign character that the diagnosis was made certain only by the characteristic appearance of the sputum and the determination of the presence in it of influenza bacilli. The patients usually, but not always, were taken suddenly with more or less severe chill, pains in the loins, back, and extremities, and almost without exception complained upon admission to hospital of severe headache. Some had severe pleuritic pains in one or the other side of the chest, and usually they presented a picture of persons who were seriously ill, and the rapid respiration and cyanosis pointed to the lungs as the seat of the trouble. The pulse was frequent, the temperature was high, 40° C. (104° F.) or over, often with morning

remissions; there was anorexia and commonly also constipation, but profuse diarrhœa was never noted. The changes in the lungs varied according to the length of time the patient had been ill, but were always very characteristic. In no case, even in the early stages of uncomplicated influenza, did Beck fail to find pronounced physical signs in the chest. In very early stages of bronchopneumonia he usually found in the posterior inferior parts a dulness on percussion with well-marked bronchial breathing (which was itself, however, very characteristic, as if it were transmitted from a distance) and fine and coarse bubbling râles. In other cases the entire process was located at the apices and a physical examination revealed a picture more like that of a tuberculous affection of the apices, but which disappeared entirely after recovery from the influenza. In other cases again the symptoms resembled those of wandering pneumonia, the affection involving first the entire left lower lobe, for example, and then passing over to the right upper lobe while resolution was taking place in the lower lobe. Always, however, the same characteristic physical signs were present, namely, pronounced dulness on percussion over the affected portion, with distant bronchial breathing and râles of various sorts. In the stage of resolution the bronchial assumed gradually the character of vesicular breathing, and more or less coarse bubbling râles were audible.

I shall quote here the history of a case reported by Beck, as it presents very clearly the morbid picture which he regarded as characteristic of the bronchopneumonia of influenza; indeed he calls it a typical case of grippal pneumonia.

A robust man, 28 years of age, previously in good health, was seized on November 25th with a chill followed by a feeling of heat, severe headache, a feeling of extreme fatigue in the limbs, shortness of breath, and frequent cough with expectoration. Upon admission to the Institute three days later, he complained of vertigo, dyspnœa, weakness, and troublesome cough. His face was flushed, the pulse was rapid, and respiration was deep and labored. Examination of the chest revealed dulness, bronchial breathing, and moderately coarse bubbling râles posteriorly at the base of each lung. Over both lungs expiration was sharp and prolonged and was accompanied by sonorous and whistling râles. The expectoration was profuse, of a yellowish color, and contained numerous influenza bacilli. A few days later, on December 4th, the dulness on the left side had extended upwards the width of a rib, over the dull portions were heard coarse bubbling râles, and at the same time there were crepitant râles and signs of bronchial catarrh at both apices. The patient felt a little better than on admission. On December 6th many fine and coarse bubbling râles were audible over the dull areas posteriorly, while anteriorly there was very evident dulness on the right side

both above and below the clavicle. Five days later the dulness posteriorly had cleared up, but there were still to be heard some crepitant râles together with slight bronchial breathing. On December 14th the dulness and râles anteriorly had entirely disappeared, but posteriorly there were again some faintly dull areas in which could be heard coarse bubbling râles mingled with crepitation. The temperature up to this time had ranged from 37° to 38° C. (98.6° to 100.4° F.) in the morning and from 39° to 39.5° C. (102.2° to 103.1° F.) in the evening, but at this time it fell to from 36.5° to 37.3° C. (97.7° to 99.1° F.). The patient now felt quite well, but he still had considerable cough with expectoration. He was discharged cured on January 2d. Influenza bacilli were found as late as December 21st.

It is now of common observation that the pulmonary tissue becomes infected from the bronchi, in influenza, and so bronchopneumonia arises. This is easy to understand from what we know of the influenza bacillus; indeed, it is a cause for wonder that such extensive bronchial catarrh may often exist without leading to bronchopneumonia, especially as the secretion within the tubes is profuse, thin, and frankly purulent. True bronchopneumonia is the most frequent pulmonary affection in influenza, and Pfeiffer has shown in his work on the etiology of influenza that in such cases the grippal process invades the lungs from the bronchi. His preparations show very clearly how the ciliated epithelium in the larger branches is destroyed, how the epithelial shreds are found lying in the lumen of the bronchus, and how in other places the epithelium seems to be raised up by pus cells formed beneath it. He describes how the pus cells force their way in little masses between the cylindrical cells, even when the epithelial coat is apparently infact, fill the defects caused by the loss of ciliated epithelium, and cover in a more or less thick layer the free surface of the mucous membrane. The peribronchial connective tissue contains many wandering cells. Similar changes occur also in the smaller bronchioles, the lumen of which, Pfeiffer says, is usually completely filled with mucin and pus corpuscles. He found influenza bacilli in enormous numbers in the bronchi on the epithelium and between its cells, and also beneath this layer. He believes that the wandering cells come to the free surface of the bronchial mucous membrane and there load themselves with influenza bacilli, producing the characteristic mucopurulent secretion of grippal bronchitis. "The entire process therefore appears in the guise of a catarrhal suppuration in optima forma." The course of this inflammation is a progressive one, from the nose or larynx downwards, extending by continuity to the pulmonary tissue. "In this circumstance we find a satisfactory explanation of the lobular character of grippal pneumonia. Each area of infiltration is to be regarded as in relation with

a diseased bronchus through which the infectious agent has gained access to the pulmonary tissue." Beck explains the origin of the pulmonary inflammation in exactly the same way in his work on influenza pneumonia, asserting that the preliminary process takes place entirely in the air passages, especially in the bronchi, and then the inflammation invades the lungs. Pure, uncomplicated grippal pneumonia, he says, is a true bronchopneumonia of a suppurative character.

The observations of Pfeiffer and Beck are so unmistakable that they permit of no other conclusion, and we all know that clinically a bronchitis occurring in influenza leads with extreme frequency to pneumonia. In my work on the acute pulmonary inflammations I have remarked upon this in the following terms: "In 1889 and 1890, during the great influenza epidemic, we had to treat a surprisingly large number of cases of bronchopneumonia. The affection of the bronchial mucous membrane belongs almost without exception to the 'catarrhal' form of grippe; the consecutive pneumonia is in many cases fibrinous, in others cellular, in others again a bronchopneumonia with more or less catarrhal exudation." A very interesting paper on "Cellular Infiltration of the Lungs, or Cellular Bronchopneumonia," was read by Dr. W. C. Glasgow, of St. Louis, before the Missouri State Medical Association in 1891, which I will note here, as this author seems to me to have been one of the first to have understood correctly this form of bronchopneumonia. He states that he saw the first cases of this sort in the winter of 1886-87, and since then has met with them, sometimes in large number, sometimes only as isolated instances. With the appearance of influenza in the autumn of 1889 they became very common and were called "grippe pneumonia." But he asserts with positiveness that these differed in no way from the cases which he had been observing since 1886. He assumes, therefore, that influenza existed there four years before its outbreak in Russia. The extreme contagiousness of this form of pneumonia is well shown by him by the following striking example:

"In the beginning of April this bronchopneumonia appeared [in Bethesda, a foundling hospital in St. Louis], and within a few days every baby of the thirty in the nurseries was attacked with the disease, with the exception of those who were kept in another part of the building. Thirteen died. In all cases the attack was sudden, even in the most healthy babies. The temperature rapidly rose to 105°, and several died after a few hours' illness, in convulsions. The capillary bronchitis type was the most frequent. Two died with the signs of acute emphysema, great dyspnœa, but no cyanosis. While the nurseries were being disinfected the babies were removed to an

adjoining building, and an improvement was at once evident. After disinfection, the babies were returned to the nurseries and the improvement still continued. A new healthy baby was received and placed with the sick ones, and in twenty-four hours she showed the symptoms of the disease."

The following case, which was under observation during the entire course of the disease, illustrates well some of the statements above made.

The patient was admitted to the Friedrich-Wilhelm Stift in Bonn on account of disease of the heart, and a few days later, on December 24th, 1889, was taken with the usual symptoms of influenza, which he had probably contracted from his neighbor in the ward, who was suffering from a severe grippal pneumonia, from which, however, he recovered. The axillary temperature ranged during the first few days from 37.2° to 38.8° C. (99° to 101.8° F.). On the evening of December 28th the temperature rose to 39.9° C. (103.8° F.), and during the night there was a profuse sweat. The following morning the temperature fell to 37° C. (98.6° F.), the pulse was 100, very small, and soft. There was dulness on percussion, with crepitation in the upper portion of the right lung posteriorly. The respiratory murmur was not audible. In the evening the temperature rose again to 38.4° C. (101.1° F.); the next morning it was one-tenth of a degree lower and the pulse was 120. There was marked dyspnœa, but expectoration was scanty. There was now dulness posteriorly over the entire right side and crepitation was heard over the dull portion, but no bronchial breathing; slight crepitation was audible over the lower margin of the left lung. There was tympanitic resonance for a space 3 cm. wide over the liver and above this on the right side anteriorly was clear resonance with a few bronchitic râles. The evening temperatue was 39° (102.2°), but this fell to 37.6° (99.7°) the next morning and to 37° (98.6°) the following evening. The patient remained about the same up to January 3d. On the morning of this day the temperature was 38.3° (101°) and examination revealed dulness over the middle lobe of the right lung. Posteriorly bronchial breathing and crepitant râles were heard over the areas of dulness, and diminished respiratory sounds over the middle lobe. The liver was painful and somewhat enlarged. The heart sounds were distinct, the apex beat was diffused, the pulse was 140. The feet were swollen. The evening temperature was 39.4° (102.9°). The sputum was the color of raw beef and was more or less frothy. The next day the evening temperature rose to 40° (104°), the pulse was 120 and irregular, respiration 40; there was marked dyspnœa and rattling sounds were plainly audible. The sputum was yellowish in color. There was dulness at the left apex, less marked under the clavicle, passing into tympanitic resonance at the level of the third rib, and becoming dull again at the fourth. On the right side there was dulness on percussion at the apex, slight tympanitic resonance under the clavicle, and dulness again at the level of the third rib. The liver dulness extended to the umbilicus, the liver itself was palpable, hard,

and sensitive. On auscultation bronchial breathing was heard on the right side above, and loud tracheal respiration with crepitant râles from the third rib and also over the hepatic border. On the left side the sounds in the upper portion were the same as on the right side; below there was sharp, but not bronchial breathing. The heart sounds were clear, the second pulmonary sound not increased. The percussion note was tympanitic but muffled at the upper portion of both lungs posteriorly; below there was a clear area, with spots of dulness interspersed, on the left side, and absolute flatness on the right side. There was pectoral fremitus on both sides. Towards evening bronchial breathing was audible over both apices, distant and faint bronchial breathing below on the right side, and crepitant and bubbling râles on the left side below. The pupils were dilated; the urine deposited a thick sediment. The patient died on January 5th. The autopsy revealed the following: The left lung contained air. The upper lobe of the right lung contained air, the lower lobes were almost entirely hepatized. Cut sections were almost entirely smooth and of a dark brownish-red color, only here and there were isolated patches of lightly granular structure. The lobular divisions were distinct, and the individual lobules were varied in appearance, some being dark, others lighter, and some seeming to be moderately aërated. The spleen was about twice the normal size, soft, and succulent. The exudate in the right lower lobe was rich in cells and contained but little fibrin.

This case was one of great value as regards its pathological anatomy, for it was one of catarrhal pneumonia as shown not only by its lobular distribution, even when there was infiltration of an entire lobe, but also by the absence of any evidence of fibrinous inflammation. The following report of an autopsy will serve to explain some of the clinical symptoms, and especially the physical signs, in cases of this sort. The autopsy was made by Beck on the body of a man who had been a hard drinker, and who died in delirium three days after admission. He had well-marked grippal bronchopneumonia in both upper lobes, marked by dulness, bronchial breathing, and coarse bubbling râles. The upper lobe of the right lung contained no air, it was flabby, and from the cut surface exuded a large amount of a turbid brown fluid. A large number of lobules, for the most part forming small groups, presented a light grayish-brown color, but were not distinguishable by the feel from the surrounding pulmonary tissue. Near the anterior border the lung substance was somewhat harder and infiltrated, and here the bronchi were dilated and filled with thick pus. In the left lung the same changes were found, only somewhat less pronounced. The pus filling the bronchiectases contained pure cultures of influenza bacilli as did also a purulent exudation covering the anterior surface of the lung. In sections of the pulmonary tissue, stained with Ziehl's solution, Beck found a

large number of pus cells in or near which were aggregations of influenza bacilli. Singularly, in the peribronchial tissue were only small collections of cells, and the mucous membrane and entire walls of the smaller bronchi, which were filled with pus cells, showed no or only slight pathological changes. At most there was only an increase in the number of leucocytes here and there. The pus cells themselves lay free without any fibrinous formation in the smaller bronchi, and the use of Weigert's fibrin stain gave negative results.

It yet remains for us to analyze the individual symptoms of grippal pneumonia. Of the physical signs the dulness interests us first. In the examination of a severe case of influenza, the signs of bronchial involvement often stand out very markedly, as was remarked above. The question is now when, in such cases, can we determine from the physical signs that a pneumonia has supervened. The areas of dulness which are discoverable in the lungs of such a patient are seldom very pronounced unless they have existed for some time. These areas are in most cases quite numerous; they are not sharply defined, but the dulness shades off indistinctly into vesicular resonance. They do not usually occupy an entire lobe, and their favorite seat appears to be at the borders of the lungs; many authors say that they are found more frequently in the left lung than in the right, while others say that the apices are most often involved. It may be that these areas of dulness are in part an indication of patches of atelectasis, which may readily arise from the plugging of individual bronchial tubes, but which are probably due in most cases to an inflammatory process.

Of especial importance among the other physical signs is the way in which the respiratory murmur is altered. Bronchial breathing is in general neither so frequent nor so regular as Beck asserts. There are many places where dulness is found in which the respiratory sounds are very weak or cannot be heard at all. When the breathing is bronchial it has the character noted by Beck of coming from a distance. The absence or diminution of respiratory sounds in the area of dulness can be readily understood when we consider that the bronchi leading to the parts may be occluded either by swelling or by the profuse secretion. Pure bronchial breathing, such as is heard in croupous pneumonia, is very uncommon, and this is a consequence of the nature of the inflammatory process. We have already shown above that marked bronchophony, upon which Leichtenstern especially lays such emphasis, is a valuable symptom in enabling us to determine the existence of infiltration in an area of dulness, even when the latter is exceedingly slight. Unfortunately, however, when

the larynx is affected the voice becomes so feeble that it is impossible to elicit bronchophony.

Wintrich describes *crepitation* under the name of vesicular râle; and as a matter of fact this designation appears to me to be a very well-chosen one, since it conveys the idea that the sound stands exactly in casual connection with the vesicles of the lung. The sound is a homogeneous one and gives one the impression of being caused by the bursting of an infinite number of air bubbles of uniform size. According to Laennec and Skoda the existence of this sound presupposes fluid in the smallest bronchi and pulmonary vesicles, which, moved by the penetrating inspiratory current of air, that naturally must be sufficiently strong, gives rise to this sound. With this Laennec coupled the idea that it was a sign pathognomonic of the first stage of pneumonia, and on the basis of this assumption he also called the râle inflammatory crepitation. This pathognomonic significance was, however, at a later period opposed by Andral, Cruveilhier, Chomel, Barth, Roger, and Skoda, so that for a long time it was sought to explain the production of this crepitation in another manner, either through the presence of an exudation in the tissue (Walshe), or as caused by ordinary adhesion of the walls of the alveoli or smallest bronchi and their tearing apart upon inspiration (Traube). Wintrich offered and proved experimentally a very ingenious explanation of the production of this sound. He declared that crepitation is simply the murmur caused by the sudden tearing apart of the mucus of the adherent walls of the smaller bronchi and alveoli by the inrushing air current. Nominally the lungs cannot contract to such a degree that the alveoli and fine bronchi adhere to each other. Therefore in a healthy condition of the lungs true crepitation can never arise. If, however, the mucous membrane of the alveoli and finest bronchi is swollen and covered with a tenacious mucus or a tenacious pneumonic exudate, then during expiration such an approximation of these that an adhesion takes place is easily conceivable. If a sudden strong inspiratory current of air sweeps into the lung during the dilatation of the alveoli and finest bronchi, then in a likewise easily conceivable manner would these adherent regions be torn apart during the rapid expiration, and cause the sound. Wintrich declares that the crepitation in various individuals may assume a varying intensity, and also that the strongest expectoration and the most intense coughing have absolutely no effect upon the crepitation, inasmuch as a sufficient swelling of the mucous membrane and a covering of this with tenacious mucus is all that is necessary for the production of crepitus. We can never cough dry such a mucous membrane, nor abolish its swelling by coughing.

In the same manner it would be easy to explain that this crepitant râle may be heard in the posterior regions of the lungs in other conditions than pneumonia; for example, in convalescence from typhoid and other severe diseases during which the patients have remained upon the back in quiet respiration for a long time. It is to be noted, however, that this non-inflammatory crepitant râle disappears after a few deep respirations. Wintrich says that the crepitant râle in the beginning and in the resolving stages of pneumonia is louder and more intense than he has ever heard it in œdema of the lungs, or, a few cases excepted, in capillary bronchitis.

In emphysema crepitation is also heard now and then. The fine râle which is called subcrepitant, is due to the presence of fluid in the smaller bronchi (Wintrich). While, therefore, crepitation is not a pathognomonic sign of pneumonia, it is at any rate very prominently found in this condition, and for our cases it will be corroborative of a pneumonia, when the causes of œdema of the lungs in an existing emphysema and collapse of the lung, such as may exist in convalescence, are excluded. It is differentiated from the crepitation of capillary bronchitis in that it is limited to certain regions, and there are no bronchitic symptoms in other parts of the lungs. It appears to me a secondary consideration whether we regard the crepitation as simply and solely originating in the vesicles of an area of the lung, or whether we also look upon it as produced in the capillary bronchi of a limited area of the lungs.

In many of the mildest cases of grippal pneumonia the entire course gives the impression as if in the general influenza infection there had been but a small, in fact incidental, localization in the alveoli; just as in other cases a mild affection of the nasal mucous membrane produces secondary symptoms. If at the same time fever exists, which in some cases reached over 40° C. (104° F.), then this does not necessarily correspond to spreading of the pneumonic process, but belongs to the simultaneously existing influenza. A remarkable feature of these cases is the extraordinarily small and frequent pulse. The repeated slight chills and sweat indicate the influenza infection which, also in cases in which no pulmonary symptoms exist, present these uniformly frequent alternations between heat and cold. The chills follow one another altogether too frequently for us to be able to refer them to recurrences of a pneumonic affection.

Among the remaining symptoms of grippal pneumonia the course of the fever strikes us most. In all, even in fatal cases, no very high temperature or at any rate no long-continued temperature is seen. The temperature ranges between 38.5° and 40° C.

(101.3° and 104°), but for the most part is under 40°, so we see that the disease bears a close resemblance to other grave infections, which, as in diphtheria, may lead to death without a high temperature. This condition of the temperature has also been noted by Stintzing. There is no definite fever type and especially no relation between the height of the fever and the gravity and extent of the local process. Even the extension of the inflammatory process is not always accompanied by an elevation of temperature. A genuine initial chill does not belong to the fever of an influenza pneumonia. If this begins at the time when the grippe symptoms are in full blast, then we simply find the repeated chills and sweats of grippe. If it arises later in the course of the disease or during convalescence, then as a rule it is not ushered in with a chill. Dyspnœa is a symptom which is much more apt to draw our attention to the pulmonary process. I have often noticed that, even without any actual increase in the rate of respiration, a great air hunger existed, but there is no constant relation between the degree of the dyspnœa and the number of respirations. Cyanosis sometimes rapidly increases towards the end of life, so that in the dyspnœa, the cyanosis, and the cold sweat we have formed a picture of complete collapse. The symptoms on the side of the heart which show themselves in the frequency and the weak character of the pulse are not caused by demonstrable disease of the heart muscle, nor is it endocarditis or pericarditis which overburdens the heart, but we can only account for it by the fact that some poison exists which affects the respiratory centre and that of the heart. The *sputum* is rarely of the character seen in croupous pneumonia. Upon this point Stintzing agrees with me in the main. In certain cases in which this author noted a sputum which really resembled that of pneumonia it is most likely that a croupous pneumonia actually existed. In other cases he describes a rich mucopurulent, not bloody sputum.

Beck describes as characteristic the fact that the sputum which is regularly expectorated in large amounts has during the height of the pneumonia, and also for a long time during convalescence, a yellowish or yellowish-green color and a tenacious mucous character, so that very frequently it is expectorated with great difficulty by the patient. In the sputum he finds at the height of the disease the influenza bacilli in pure culture, very frequently in the interior of pus cells. They can be found in the sputum for a long time during convalescence, in fact long after, when the patients feel perfectly well, and finally suddenly disappear. In such pure influenza bronchopneumonias Beck never saw rusty sputa and never found the diplobacilli of Fraenkel.

Among the studies which were undertaken in reference to true bronchopneumonia caused by the influenza bacilli alone, we must here mention particularly those of Wassermann, in which he was enabled to show that in a large majority of cases the influenza bacilli alone were present, without any admixture with diplococci and streptococci. The question then is in reference to pure uncomplicated cases in which the pneumonia sputum presents a pure culture of influenza bacilli. Therefore such a pneumonia which is of frequent occurrence during an epidemic of influenza, according to Wassermann, is not another complication of influenza, but an ordinary extension of one and the same process from the bronchi to the tissue of the lung. For that reason the bronchopneumonia of influenza stands out as an independent form of the disease, a form which particularly has nothing in common with croupous pneumonia, and is not called forth, as in the latter case, by the diplobacilli of Fraenkel. Wassermann, whose opinion is entirely in accord with that of Beck, emphasizes this point and corroborates these conditions in all of the later cases which have come under his observation since then. The sputum was never rusty, but always frothy and purulent; the fever type was irregular, and defervescence always took place by lysis. Wassermann draws our attention to the extraordinary delay in resolution in comparison with that of croupous pneumonia. As an example of this he cites the history of a woman thirty-one years of age suffering from a typical double influenza pneumonia. The woman, who was admitted March 19th, 1893, stated that she was taken ill on March 10th. The physical and other signs pointed unmistakably to grippal bronchopneumonia. Resolution did not begin until April 5th, and then proceeded so slowly that on April 14th numerous râles and dulness could still be found on the left side posteriorly. Wassermann considers this form of the disease the most frequent in influenza, in comparison with which croupous pneumonia is of exceedingly rare occurrence. We will deal with this complication later. The great majority of investigators are convinced of the fact that this bronchopneumonic form of inflammation of the lungs, which is caused by the influenza bacilli alone, may be observed. The various differences of opinion which existed before the discovery of Pfeiffer depend in part upon the fact that in the occurrence of bronchopneumonia we encountered a new symptom. Leichtenstern rightly says that physicians have suddenly found themselves confronted with a new disease in the cartarrhal bronchopneumonia of influenza, an affection which up to the recent epidemic of influenza we had regarded as always secondary, occurring in measles, diphtheria, pertussis, rickets, or in the later stages of typhoid fever, and then

practically only in children, the aged, and the enfeebled. With the appearance of influenza, however, bronchopneumonia suddenly began to be encountered as a primary acute disease attacking the young and strong and those who until then were perfectly well. Up to that time we had been taught to believe, and rightly, that every acute, even if atypical, pneumonia occurring in individuals of this class was necessarily a croupous one. The positive proof that this pneumonia is caused by the influenza bacillus can only be shown at the bedside by the finding of the specific bacilli, and this proof has been made, so that now the picture of grippal bronchopneumonia in its pathological, clinical, and etiological relations must be looked upon as finished and perfected.

Pneumonia without Bronchitis.

We will here describe certain cases in which, during the course of grippe, a pneumonia is developed without any coincident bronchitic affections. I early had my attention directed to these cases, and at the very beginning of the influenza epidemic of 1889 was much surprised to find how frequently I could demonstrate changes in the lung tissue. Within a few days after the appearance of influenza in Bonn, I saw three patients at the polyclinic in whom, in addition to the general symptoms of influenza, I was able to demonstrate consolidated areas in the lung with abundant crepitation—in one case an entire lobe being involved—without a suggestion of fluid râles or tenacious mucous sounds indicating a participation of the bronchial ramifications in the inflammatory process. Immediately after seeing these I encountered four other patients who presented general symptoms of influenza, in whom, in each case, one or more pneumonic areas could be demonstrated. All these cases were very ordinary in their nature and course, except one, that of a cabman—which on account of the severe effect of exposure to bad weather, was very much prolonged, and was marked by dulness in the affected lobe of the lung. Naturally the question may be asked, with what right we regard these cases as pneumonia.

We diagnose this from a diminished resonance of the percussion note and the presence of crepitant râles, in other cases from the crepitant râles alone. I have often in other cases convinced myself that this symptom is really to be looked upon as the beginning of a pneumonia, and in proof of this belief would recall the subsequent course of many cases of influenza pneumonia. If the process does not come to a standstill, then we can observe from hour to hour the advance of the symptoms from a beginning slight crepitant area to all the signs of a severe pneumonic process. This condition could

only be confounded with an atelectasis, which in adults, in the absence of bronchitis or even at times of cough, could readily be excluded. That nothing more than a bronchiolitis was present I dispute, because we hear the same crepitant râle in the first stage of the development of a croupous pneumonia. In the course of influenza I have very frequently seen catarrh of the bronchi and bronchioles, which in fact remained limited to a very small area or often enough to one lobe of the lung. These, however, do not cause crepitant râles, but bronchitic râles, even if very small and for the most part sibilant and sonorous râles. In the course of influenza or at other times I have never seen a bronchitis begin with this fine crepitant râle, and for that reason I feel justified in attributing the origin of the crepitation to the alveoli and in looking upon these fine crepitating areas as pneumonic in character.

These cases often run their course, from beginning to end, without a suggestion of expectoration, and as therefore cough is absent or very slight, I am convinced that very many of them in which there are limited areas of consolidation escape the observation of physicians. The following are a few examples of this mildest form of influenza pneumonia as it was seen in the first epidemic of 1889 and 1890.

In one family the mother and her little daughter were ill with influenza pneumonia and severe bronchitis; a healthy young girl of eighteen assisted in nursing them. On January 20th the latter complained of general malaise, heat in the head, pain in the left side, and dyspnœa. The evening temperature was 39° (102.2°), pulse 100, respiration 28. Examination of the chest revealed crepitation over the entire left lower lobe posteriorly, with slight dulness but without altered respiratory sounds. The following day the temperature ranged from 38.8° to 39.2° (101.8° to 102.5°), pulse 96, respiration 24. On January 24th, the temperature was 37.3° (99.1°). Up to this time the condition had remained about the same as on January 20th, the crepitation was still present, but the dulness had slightly increased, the breathing became bronchial in certain places. There was no expectoration. From January 23d, the general condition was essentially better. Gradually declining, all the symptoms had disappeared by January 26th. The normal condition returned again very rapidly.

Scattered through the city I saw four other cases very similar to this one, the only difference being the longer or shorter duration of the fever. The localization of the crepitation, the dulness, and the more or less altered breathing in circumscribed areas of the lungs, at the same time the existence of the normal condition of the bronchi, which did not show the slightest sign of a diseased mucous membrane, give these cases a fixed stamp. It is, however, very striking

to note how rapidly the various areas of the lung change, how the crepitation may disappear from hearing and then reappear. Many such mild cases came under my observation in the Friedrich-Wilhelm Hospital in Bonn.

E. F—— had been in the hospital on account of anæmia and gastralgia; temperature always normal. On the first of January he complained of headache, pain in the back and eyes, repeated chills, and fever. The temperature on this and the two following days was very slightly elevated, but then fell to normal. On the evening of the first day crepitation appeared in the right as well as in the left lower lobe. On January 2d there was slight dulness at the right apex, with increased breathing and crepitation. On January 3d, during the time the temperature was normal, the dulness remained in the right upper lobe; crepitation disappeared; during the next six days the dulness in the upper lobe disappeared entirely. In both regions posteriorly the crepitation also entirely disappeared after two days, without further changes.

The patient who was in the adjoining bed, O. W——, was received on December 28th. His temperature upon admission was, morning 38° (100.4°), evening 39.5° (103.1°), and then gradually declined until January 1st, when it became normal. Upon admission the right apex showed dulness to the third rib, gave crepitant râles and bronchial breathing. All the other regions of the lungs and bronchi were normal. While at the beginning there existed but little expectoration, on December 30th it began and became extraordinarily profuse; the sputum was always purulent, of a light yellow color, without any admixture of brown or red. The dulness was demonstrable in the right apex until January 20th, so that examinations for tubercle bacilli were repeatedly made, but always with negative results. From January 20th, in the course of a week, the dulness with all the other symptoms had entirely disappeared, and the patient was discharged as cured.

In another bed of the same room lay J——, admitted December 30th on account of headache, pain in the back, and a general bruised feeling; insomnia was complained of. The temperature remained normal until January 4th, then rose in the morning to 39° (102.2°), and on the same day, in the left lower lobe, crepitation and dulness developed, which lasted for about a week, then disappeared without any pneumonic sputum being expectorated during this time. During the apyretic period the pulse did not go below 100.

I saw fourteen such cases in the epidemic of 1889 and 1890, which are all to be looked upon as the mildest form of the pneumonia under question and which I mentioned here particularly because they demonstrate most clearly the real disease beginning in the alveoli or their immediate neighborhood without any bronchitic complication. I also saw the same disease in the influenza epidemic of 1893 and 1894.

In the surgical division of the Friedrich-Wilhelm Institute there lay in January, 1894, a patient who, during the time other cases of influenza came to the hospital, was infected there. On the 21st of January, 1894, he suddenly became very hoarse, coughed severely, and complained of headache and pain in the left side, especially in the left infraclavicular region. Here the percussion note was slightly diminished, the expiration was prolonged, and bronchophony was present. Two days later sibilant breathing and râles were heard and at the same time there appeared quite an amount of purulent expectoration. Upon microscopical examination this was seen to swarm with influenza bacilli. On the fifth day after the acute onset, however, only a few influenza bacilli could be found in the expectoration, and no other bacteria were present. All of the symptoms rapidly diminished, cough and expectoration soon became very slight. The sputum was slight in amount, but remained of a purulent character, and three weeks after the beginning of the acute influenza no influenza bacilli could be demonstrated either in the specimen or in the culture.

V. D. H——, admitted on December 16th, 1889, was taken ill during the night of the 14th with nausea and marked weakness. Towards three o'clock in the morning he had repeated chills, and these alternated with intervals of sweating during the following day. The headache and pain in the back became very marked. On admission the temperature was, morning 39.7° (103.4°), evening 39.5° (103.1°). The next day the temperature fell to normal without marked sweating. Upon admission there were somewhat increased breath sounds in the lower part of the left lung posteriorly, but the remainder of the lung appeared normal. On the morning of the 17th, after the fall of the temperature, there appeared under the angle of the left scapula slight dulness over an area the size of the palm of a hand, with blowing respiration without any crepitation. This area remained until the following evening. At the same time there were great restlessness and cough without expectoration. Following a very restless night, the patient complained of severe headache on the morning of the 18th. The expectoration consisted of a tenacious mucus at times of a brownish color. On the right side the percussion sound was normal up to two fingers' breadth from the border of the liver, where a distinct tympanitic zone existed. On the left side the tympanitic note of the stomach was heard as far up as the fifth rib, in the anterior axillary line, and above this region dulness existed which increased posteriorly. Pectoral fremitus was diminished in this region. Posteriorly there was a clear note as far as the sixth rib, from there downward dulness with a tympanitic character and distinct cracked-pot sound. There was also slight dulness over the corresponding region of the right side. The breath sounds were normal over the upper portion of the left lung posteriorly, but from the fifth rib downwards they were loudly bronchial, without, however, any crepitation, even at the edge of the area of dulness. Pectoral fremitus was increased over this region; beyond this the percussion gave nothing abnormal. On December 21st the morning temperature was 39° (102.2°), pulse 80, evening 38° (100.4°). The entire left lower lobe gave dulness and crepitation. During the night a quiet

sleep set in, and on December 22d the temperature was normal and so remained. The resolution of the pneumonic process in the lower lobe took place completely in six days. Slight dulness could be elicited on the right side posteriorly for four days more and then disappeared without crepitation. On January 5th the patient was discharged as cured.

This case was one of consolidation of the left lower lobe, subsequent to a pneumonia in the upper lobe. Even before this there were changes at the base of the upper lobe and the corresponding region on the right side, and apparently later in the centre of the right lobe. In spite of the fact that these areas had previously established themselves, the others developed most fully and diffusely in the left lower lobe. This pneumonic process, which had led also to general infection as shown by enlargement of the liver, diarrhœa, and excessive meteorism, lasted eight days before the decline of temperature appeared. The retrogression to the normal did not take place by means of an outspoken crisis, in that the critical symptoms were unaccompanied by sweating, but by lysis in which the decline, though rapid, takes place intermittingly.

B——, a man 68 years of age, who two years previously had a croupous pneumonia of the left lower lobe, showed the symptoms of influenza on January 4th. Under repeated chills and perspiration the temperature rose to 39.5° (103.1°) in the evening. The pulse became remarkably soft and reached 120. The next morning the temperature was 40° (104°); there was considerable shortness of breath, the pulse was 120, respiration 36. The examination showed, on the right side, anteriorly above the liver, an area the size of the palm with crepitation, without distinct dulness. The temperature remained 40° C. in the evening, and continued for three days between 40° and 40.5° (104° and 104.9°). During this time the pneumonic area extended posteriorly so that a large part of the right lower lobe was implicated, but to the right of the vertebral column a strip of three fingers' width gave complete resonance. The dyspnœa continued just as in the beginning. Great restlessness, insomnia, and a feeling of apprehension disturbed the patient, and while the infiltration advanced posteriorly, the dulness over this entire area became more intense. There was no increase of the pectoral fremitus. The crepitation disappeared four days after the extension of the dulness; the breathing remained diminished posteriorly, but was not distinctly bronchial, while anteriorly over the region first attacked it assumed a blowing character. The pulse became constantly worse, the abdomen was tympanitic, the liver was painful to palpation and swollen through congestion. The urine was scanty and contained a trace of albumin and an abundant sediment. The sputum remained—as from the beginning—of a tenacious and mucous character without showing any distinct coloration. On the seventh day tracheal râles set in, followed by bilateral pulmonary œdema, and death occurred in collapse.

The cases described above will serve as examples of the fact that influenza pneumonia does not lead rapidly to the development of considerable areas at the originally affected regions, without assuming very clearly the character of a wandering pneumonia. In the following cases this wandering type of pneumonia was very striking.

V——, a tradesman 28 years of age, has been feeling unwell since December 31st; he complains of vertigo, sleeplessness, without, however, any particular pain. There were numerous chills with sweating, and the man took to his bed on January 2d. For eight days before he went to bed the patient was hoarse, but had no cough. The disease did not begin with an actual chill, but a restlessness during the night of January 1st to 2d called the attention of the patient to the fact that he was really more ill than he at first thought. Under the development of these gradually advancing symptoms a pneumonia of the right lower lobe, in the most dependent portion of the same, was developed. The temperature ranged from 38° (100.4°) to 39.3° (102.7°). On January 4th the entire right lower lobe was shown to be diseased, but in a very peculiar manner. First of all the dulness over the entire extent of the lower lobe was very slight; over certain regions, namely, where the crepitation first appeared, faint bronchial breathing could be heard. Around those areas where the dulness was in reality still more distinct, no breathing could be heard, and at the border of the entire process, anteriorly and superiorly as well as laterally, crepitation was heard. The regions in which one day there was crepitation, the following day were dull on percussion without crepitation. Here and there bronchial breathing could be heard; in other places breathing was absent. During the next three days the process advanced farther in the upper lobe and extended as far as the spine of the scapula, whereas the apex remained free. Nothing was noticed in the right apex anteriorly, but from the third to the fifth rib there developed on January 10th a new area, which in the course of three days reached proportions as great as the lesion which previously had attacked the lower lobe. During this time the temperature did not exceed 39.5° (103.1°); the pulse, however, became smaller and never fell below 120. The liver was swollen and painful, the splenic dulness was increased, and the spleen was palpable at the free border of the ribs. On the eleventh day of the disease, a new area developed at the border of the left lower lobe posteriorly, and while the previously mentioned areas of the right side did not grow any larger, those of the left side extended farther upwards so that in the course of five days practically the entire left lower lobe was involved in the process. The signs here were the same as on the right side; the dulness was not very marked, bronchial breathing could be heard only here and there, and pectoral fremitus was not increased. At the edge of the inflammation crepitation could always be heard over certain regions. While these various pneumonic areas extended according to the type of wandering pneumonia, the strength of the patient materially decreased, so that the heart's action was sustained only by means of large amounts of alcoholic stimulants. The fever lasted until January 20th, at which

time the pneumonic areas were reabsorbed, without any distinct crepitation or other signs of resolution. During this time the sputum was far less in amount than during the development of the areas. At that time it was tenacious, slightly brown, at times of a rose or raw-meat color. The patient remained in bed until February 1st. During the period of fever he was frequently delirious, but so that he always knew the diseased condition of his mental state and later had a very clear recollection of the incidents during his disease. After this a very speedy convalescence followed, so that by the end of February the patient was able to return to his business.

In the following case the pneumonia developed very rapidly.

K——, alcoholic, 58 years of age, complained on Wednesday of influenza symptoms, marked headache, pains in the limbs, and nausea; on this account he remained in bed Thursday and Friday, arose again on Saturday without, however, leaving the room. On Saturday morning he felt sicker than on the previous day. Without any chill, the temperature on Sunday morning rose to 40° (104°), pulse 120, respiration 36. Examination showed three small areas of consolidation, two in the right lower lobe, and one in the left upper lobe at its base. From these three regions there developed by Sunday morning a complete consolidation of the right lower lobe and a bottle-like infiltration of the left upper lobe posteriorly; but in the same region anteriorly only a weak tympanitic change of the percussion note could be demonstrated. The morning temperature on Monday was 39.5° (103.1°), pulse 120, respiration 36; there was brown pneumonic sputum, very tenacious, here and there mixed with fresh blood. Until Monday evening the pneumonic areas remained unchanged, whereas the temperature went up to 40.5° (104.9°), the pulse reached 140, became very weak and easily compressible. During this day marked signs of mental disturbance appeared. Œdematous râles could be heard at the border of the lung and upon both sides. The pulse could no longer be counted, the restlessness increased, there was a marked cyanosis of the face, and the liver was painful on palpation. A bath at 18° C. (64.4° F.) was ordered, the patient remaining there fifteen minutes. By this means the respirations, which previously were 48, were brought down to 36. One-half hour after the bath there were no physical signs of pulmonary œdema, but the pulse remained over 140 and was of a soft, wretched character. Within one hour after the bath the former state of marked irritability was reached and the pulse became just as bad as before. Death followed five hours later, after tracheal râles, pulmonary œdema, and complete sopor had developed.

From a study of the symptoms in the cases above cited it must be admitted that the first changes may at times occur in the lung tissue itself, without a previous affection of the nose or larynx. Even though these cases are far less frequent than those in which the bronchi are affected before the lung, I have nevertheless insisted upon the fact of their occurrence and have supported my assertion

by strong proofs. I give a prominent place to the circumstance that the first crepitation is extraordinarily fine in character, such as it is wont to be at the beginning of a fibrinous pneumonia or of those forms of streptococcus pneumonia which run their course in the tissue of the lung without participation of the bronchi. Another evidence in support of my contention is that in such cases no sputum appears at the beginning, and only when resolution is commencing do we find purulent expectoration; or again, it may happen that resolution is completed without any expectoration or the appearance of bronchitic râles.

Such changes in the lungs also appear in cases of influenza in which from the beginning nervous or gastric symptoms have existed, and in which as a rule bronchitis has not developed. Such have been seen not only by me but by others. Thus, for example, Leichtenstern writes that numerous influenza patients took sick with pneumonia in whom no bronchitis of any account existed, and he particularly states it as his opinion that the bronchitis need not be a forerunner of the croupous pneumonia which so frequently complicates influenza. He especially emphasizes the fact that each division of the respiratory apparatus may be primarily diseased, without other parts being implicated in the process. Frequently he says: "There is an isolated nasopharyngeal catarrh. However, we have also observed cases in which the larynx alone was more or less severely diseased. The cases in which—either alone or preëminently—the trachea and principal bronchi were attacked, presented now and then convulsive attacks of cough analogous to those of pertussis, with loud bellowing paroxysms, which sometimes resembled suffocative fits. However, the bronchi, bronchioles, and alveoli may also be primarily diseased without catarrhal symptoms on the part of regions higher up in the respiratory tract. There exists in particular also a very acute primary influenza pneumonia, that is to say, an influenza which at once sets in with the symptoms of pneumonia."

This clinical observation is also distinctly emphasized in Drasche's work on influenza. There Drasche says: "Even though in the majority of cases of influenza pneumonia the bronchitic affection precedes, and from here the inflammatory process advances to the lung tissue, still clinical observation shows that that form may be developed without any sign of bronchitis as a direct result of infection." Yet it cannot be denied that in the presence of this kind of clinical symptoms the possibility of a primary participation of the bronchial mucous membrane always exists. Firstly, it is possible that a dry inflammation of the mucous membrane was present in the bronchi, which did not declare itself either through secretion or bronchitic

râles; secondly, it also happens that marked changes develop in the bronchi, that in fact extensive purulent secretion occurs there without producing any symptoms during life. Apropos of this I will mention a case described by Beck. A patient who suffered from sarcoma of the inferior maxilla was suddenly and without apparent cause attacked with high fever which caused his death in a few days. At the autopsy there was found a medium-sized bronchus filled with a mass of yellowish, creamy pus, which upon microscopical examination was found to consist of a pure culture of influenza bacilli. Admitted then that after such considerations the first seat of disease has its location in the bronchi more frequently than the clinical examination shows, there still remain cases in which as a matter of fact the bronchi remain free. My former communications and the observations of Ribbert at the time of the great influenza epidemic have established the fact that special changes in the bronchial mucous membrane are found almost absolutely. Ribbert designates as common to all cases a redness of varying intensity in the mucous membrane of the larger bronchi, the trachea, and in many cases also the larynx. However, he also says explicitly: "This infection was very slight in one case, which also differed somewhat from the others in that a whitish mucous froth covered the mucous membrane, which as a rule was covered rather with a tenacious gray or yellowish-green mucus."

If I combine these observations with what I have frequently seen in microscopical preparations, namely, that the finest bronchi in the centre of the cellular infiltrated lung tissue may remain entirely free, then this serves to corroborate my previous statement that the tissue of the lung may, as a result of the influenza infection, pass through primary inflammatory cellular changes whithout interposition of a bronchial suppuration. The reason why I lay particular stress upon this condition is that, if we expect only the bronchopneumonia in influenza, then these primary cellular inflammations of the lungs will be overlooked in their beginning. I have again and again convinced myself that slight areas of consolidation, which betray themselves by crepitation, occur in one or another part of the lung with extraordinary frequency, but they may be very easily overlooked upon superficial examination. From this, however, there develops often in a remarkably short time a diffuse pneumonia, which could perhaps have been prevented had the danger been recognized in time. We very frequently hear the statement made that "an inflammation of the lungs developed after influenza," and also the common observation that "the convalescent patient was taken ill with a severe protracted pneumonia," and I am very certain that the trouble might often have been avoided had those small pneumonic areas been recognized. The

statements of Leichtenstern particularly support my idea; he says: "Whereas all the symptoms (temperature, tachypnœa, tachycardia, etc.) showed the onset of an influenza pneumonia, at times it was impossible for many days to demonstrate the seat of the inflammatory area. Far more frequently, however, it was possible, after examinations which were undertaken daily and which necessitated a great expenditure of time, to find here and there, generally bilaterally, here in the lower, there in the upper lobe, in the axillary line, the lingula, or particularly often at the lower edge of the shoulder blade, an area varying in size from a silver dollar to the palm of the hand, which, marked by a relative dulness, presented numerous fine crepitations, bronchial breathing, and bronchophony. In the very numerous examinations of the thorax during the influenza period, I have learned particularly to regard bronchophony as a most valuable symptom which often helped me locate very distinctly the small infiltrated area no larger than a dollar." This bronchophony, insisted upon by Leichtenstern, can be recommended as a most excellent aid in the diagnosis of indistinct primary areas of consolidation in the lungs.

Mixed Infections of the Lungs.

Our knowledge of the streptococcus infection now explains how these bacteria occur mixed with the influenza bacilli, and how the inclination of the streptococci to such coöperation leads to epidemic mixed infection. In a similar manner, the influenza bacilli find themselves inclined to association with the diplococcus of Fraenkel. This being accepted, then the various "consequent diseases" of influenza can be understood, and particularly can the various differences of opinion upon the occurrence of the different forms of pneumonia in influenza be judged on this basis. Not only, however, has this point been settled by the results of bacteriological investigation, but it can also be demonstrated by clinical experience.

In 1837 Vigla of Paris stated that since the beginning of January, before the invasion of grippe of that year, pneumonia seemed to occur far more frequently than in the previous winters, and the course of the inflammation on the whole was out of the ordinary and atypical. Piedagnel also makes the same remark, namely, that the pneumonia of that winter no longer had its ordinary inflammatory character but showed a mixture of pulmonary catarrh, pneumonia, and pleuritis. At that time, at the height of the epidemic, the pneumonic diseases were so mixed with grippe that authors grouped the two, regarding pneumonia either, as did Nonat, Vigla, and Petrequin, as a complication of grippe or, as did Landau, Piorry, and Gourand, as the ordinary

localization of the disease. In a letter to the Paris Academy of Medicine Piorry depicted the character of the pneumonia on the authority of Ménétrier, as follows: "The pneumonia of that time differed essentially from the ordinary form; it followed bronchitis or bronchorrhœa. This form originated from the bronchi. Its beginning was slow and gradual." As for the anatomical condition, Piorry states that in addition to the genuine pneumonic changes there existed obstruction of numerous bronchi with mucus, which was either clear and frothy or thick and opaque. From this description the bronchopneumonia of our recent influenza epidemic can be readily recognized. Contrary to this, Landau states that the preexistence of a bronchitis was not constant in the majority of cases. It was absent in nine of his cases. He especially notes the frequent absence of the pleuritic pains and of the characteristic râles, the prostration of strength, the weakness of the pulse, and the intense dyspnœa out of all proportion to the extent of the inflammation, and he considers the pneumonia not a complication but an essential manifestation of the disease.

Nonat has written a work in which he admits a great diversity in the pneumonias of influenza. He distinguishes a group with severe general symptoms out of proportion to the local lesion, which he says is the same as the "malignant" pneumonia of the earlier authors and the "infectious" pneumonia of modern writers. In addition to this there is always a certain number of cases of pneumonia of the same character as those encountered at any other time. Of the latter he reports ten cases with ten recoveries, of the former nineteen and only seven recoveries. With respect to the pathological process he first describes a form in which pseudomembranes exist in the bronchi leading to the hepatized lobe, and he considers this to be a disease closely resembling croupous bronchitis, and one of the complications of influenza. The second group which Nonat describes concerns pneumonias with an adynamic course; these are the same as the first except that there are no pseudomembranes in the bronchi. He admits that adynamic pneumonia occurs at other times, but he contends that it is far more frequent during an epidemic of grippe. An extraordinary number of cases of pneumonia without any other symptoms of grippe has been described by Hourmann as occurring during that epidemic. Ménétrier shows from the study of a series of later epidemics that grippe and pneumonia are two diseases which very frequently coexist. He particularly mentions the work of Malcorps ("La grippe et ses epidémies," Brussels, 1874), chiefly for the reason that this observer's description of the peculiar form of grippal pneumonia corresponds neither to the reports of earlier dates, nor to the

cases which Ménétrier himself had seen. The description appears to me, however, to fit accurately with what I myself have seen of influenza pneumonia. He describes three stages of the disease: congestion, splenization, and gray softening. The seat of the disease is the apex of the lung, whereas the ordinary form of pneumonia attacks far more frequently the lower lobes. According to him the grippal pneumonia is far more severe and malignant. Although in this description autopsical details are absent, they are nevertheless partly compensated for by the accurate clinical description.

According to Malcorps grippal pneumonia is distinguished from ordinary inflammation of the lungs by the absence of pleuritic pains, by a much greater dyspnœa which is altogether out of proportion to the extent of the lesion, and by a dry periodic cough accompanied by a seromucous, blood-stained expectoration. Percussion gives only relative dulness over the affected region. This symptom is constant. Malcorps did not hear crepitation, but only a few fluid râles of a subcrepitant character. Bronchial breathing and bronchophony were entirely absent. The respiratory sounds were absent as a rule in the pneumonic areas. Ménétrier himself gives a very complete description of a large number of cases of inflammation of the lung which he refers to grippe. He divides these into two large groups: I. Grippal pneumonias in which recovery takes place; this is subdivided into: (1) Forms which are peculiar on account of their entire development and the anomaly of the fever curve; (2) forms with very intense symptoms, which include bilious pneumonia, pleuropneumonia, and pneumonia with bronchitis. II. Pneumonias with fatal results, which are further subdivided into (1) Infectious pneumonia running a rapidly fatal course; (2) alcoholic pneumonia; (3) bronchopneumonias; (4) pneumonias localized in scattered areas.

Among the diseases in group II. nearly all are of the croupous form. The work of Ménétrier appears to me a very important one, for the reason that a large number of autopsies are therein recorded of pneumonias that were regarded by the author as having a close relation with grippe, and in which the bacteriological examination showed the constant presence of the diplococcus of pneumonia. Ménétrier claims to have proved that we are dealing in grippe with the ordinary form of pneumonia. The anatomical changes are the same as in the pneumonias which occur independently of influenza. The pneumococci found in the sputum and blood of the living, as well as in the various areas of consolidation, are identical with the diplococci of ordinary pneumonia. If we analyze more carefully the cases which Ménétrier has described as "grippal pneumonia with fatal issue," it will be

evident that these were essentially other than such as we have seen in grippe and such as have been described, among others, by Grisolle and Nonat. The first three cases of his group began with chills. Two others, designated as bronchopneumonia, were croupous pneumonias in lungs in which old bronchitic changes already existed. The sixth case was a pneumonia with general symptoms of infection; the seventh also was a croupous pneumonia which belonged to the same group as case six, with numerous localizations, that is, metastases in the heart, etc. Excluding then the first three cases of ordinary pneumonia, we have here but to consider in comparison with our grippal pneumonias, the two cases which were designated as bronchopneumonias. According to the anatomical description these correspond to the frequently observed bronchopneumonia in chronic bronchitis.

Among the other cases of Ménétrier there is not one which can be regarded as true grippal pneumonia. The diverse forms of pneumonia in grippe are also described by Stintzing from the Munich epidemic. He regarded most of the cases as bronchopneumonias, recognized after numerous lobular areas had coalesced and the lobular had been thus converted into a lobar pneumonia. Of the seventeen cases of pneumonia which he describes he says that two positively belonged to the croupous form, whereas most of the others were catarrhal. It should be noted that Stintzing diagnosed a pneumonia only when, besides the bronchitic symptoms, marked symptoms of consolidation of the lungs were demonstrable. This limit appears to me to be somewhat too tightly drawn, for I have had a case in which a pneumonia ran its course with the characteristic sputum, and ended fatally without it being possible during life to demonstrate in what region of the lung the pneumonia—which had to be accepted with certainty because of its symptoms and course—could have had its seat. On the other hand, as has been previously mentioned, the symptoms of consolidation of the lung are often so significant that we certainly reckon the number of pneumonias as too small if we look upon that as the sole proof of an existing pneumonic process.

Leyden also has said that the pneumonias of influenza are quite peculiar. He believes that various forms of pneumonia occur, a catarrhal which belongs to the influenza as such and a croupous which runs the same course as the ordinary pneumonia. Under that which Leyden designates as catarrhal pneumonia is to be recognized the pneumonia which occurs in scattered areas. Biermer regards influenza as a collective term for a series of catarrhal forms of disease, which occur under a common epidemic influence. According to his idea,

the mucous membrane of the respiratory apparatus plays a very important part in the symptoms of influenza. The dyspnœa, which occurs so frequently in influenza, depends, according to Biermer, partly upon the croupous disease of the respiratory mucous membrane, partly upon complication with pneumonia, or also with previously existing diseases of the lung; and he is particularly inclined to attribute the disproportionate dyspnœa to congestion of the lungs. Copland, in the examination of the various diseases which appear in influenza, draws the limits of actual influenza so closely that he reckons the bronchitic, the tonsillar, and the gastric disturbances among the complications, so that according to this idea practically all severe cases must be regarded as complicated. Biermer does not go so far as to exclude these diseases from the picture of influenza, but nevertheless he regards pneumonia as a complication of influenza. So far as the character of the pneumonia is concerned Biermer says that in most cases it is preceded by a continuation of the bronchitis to the lobules of the lung and is of a catarrhal nature. "Croupous pneumonias with fully developed hepatization and croupous obstruction of the bronchi also occur in grippe patients, but are less frequent than the catarrhal form." The grippe of 1837 gave Landouzy occasion to differentiate as special forms head, chest, and abdominal grippe. We see that this differentiation corresponds to the nervous, catarrhal, and gastric forms of other authors. To these forms Lombard added a fourth under the name of intense or violent grippe, which, however, was not characterized by the prominence of one or the other local affection, but only by the intensity of the general functional disturbances. What he calls chest grippe includes influenza bronchitis, together with the intercostal neuralgias. Under the heading of chest grippe he also includes two forms of pneumonia which develop in the course of influenza. The one develops during the height of the disease in an insidious manner from a bronchitis affecting the upper bronchi, has its seat in the upper lobe of the lung, and is the real grippal pneumonia. The other attacks the patients suddenly during convalescence from grippe, that is those who expose themselves, has its seat in the middle lobe posteriorly, only on one side, and presents the signs of ordinary pneumonia with which it is identical.

As a particular characteristic of grippal pneumonia Lombard mentions the onset with repeated chills, with slight elevation of temperature, and increased rapidity of respiration. The pulse assumes neither the character nor the fulness of that of an ordinary pneumonia; the pleuritic pains are wanting, the expectoration is neither viscous nor rusty; at the most we see now and then streaks

of blood in it. Percussion does not furnish sufficient signs because, as he supposes, this pneumonia occurs in regions which are but slightly accessible to examination, such as the supra- and infraspinous fossæ. Instead of the crepitant he heard a moist, subcrepitant râle. Bronchial breathing and bronchophony were practically always absent. Delirium and continuous coma are stated to have been usual in cases running a fatal course. From the description we see that Lombard's cases were examples of multiple lobular pneumonia. His observations are of the greatest value to us, as proving that in the epidemic at Lüttich the same forms of pneumonia occurred which Gersolle then and which we now have described, namely, various forms of pneumonia occurring together in groups, here streptococci, there diplococci; here catarrhal, often if not always with lobular localization, in other regions fibrinous, as a rule lobar inflammations. All this points to the one fact that the influenza infection is very commonly coincident with other infections.

Diplococcus Pneumonia.

We can understand very well how in former times, including the period of the great influenza epidemic of 1889 and 1890, the various forms of inflammation of the lungs were grouped together without any clear distinction. But with our present knowledge we must conclude that diplococcus pneumonia occurs in a typical form in influenza. In all places where physicians have made accurate examination of influenza cases, such typical pneumonias have been observed. If these arose in the beginning of the influenza infection their symptoms were naturally modified by those of influenza. If, on the other hand, they developed at a later stage or after apparently complete recovery from grippe, they often presented the typical symptoms of croupous pneumonia. The sudden rise of temperature and the chill, the pain in the side, the painful cough, and the expectoration of a red or brown tinged, so-called pneumonic sputum, were not wanting in such cases.

Birch-Hirschfeld in 108 influenza autopsies found 11 cases of croupous lobar pneumonia. Naunyn of Strasburg has repeatedly seen true lobar pneumonia in influenza. Böllinger of Munich found among 10 cases of influenza pneumonia 5 of croupous lobar pneumonia. Marchand found 3 cases of lobar pneumonia in 5 influenza pneumonias. Finkler in 45 pneumonias observed 2 thoroughly typical cases of lobar pneumonia. Regarding fibrinous lobar pneumonia, we find an interesting communication in the work on "The Influenza Epidemic During the Winter of 1889 and 1890 in Riga," by Krannhals. The author grouped the grippal pneumonias into three classes: (1) The typical fibrinous

lobar pneumonia; (2) doubtful fibrinous pneumonia; (3) catarrhal pneumonias. He also sought to determine the numerical proportion of these three forms of pneumonia to the observed cases of influenza. He collected reports of 112 cases of inflammatory affections of the lungs in 1,687 cases of influenza, that is, 6.6 per cent. There occurred in every 100 cases of influenza 3.15 of typical fibrinous pneumonia, 1.3 of doubtful, and 2.2 of the catarrhal forms. Krannhals also collected from 70 physicians reports of 228 cases of typical fibrinous pneumonia. Of 210 of these there occurred: In October, 1889, 14 (8 men, 6 women); in November, 1889, 81 (54 men, 27 women); in December, 1889, 66 (37 men, 29 women); in January, 1890, 31 (22 men, 9 women); in February, 1890, 18 (13 men, 5 women)—210 cases (134 men, 76 women). The mortality was: In October, 1889, 3 out of 14 = 21.5 per cent.; in November, 1889, 28 out of 81 = 34.6 per cent.; in December, 1889, 29 out of 66 = 43.9 per cent.; in January, 1890, 10 out of 31 = 32.3 per cent.; in February, 1890, 7 out of 18 = 39 per cent.—a total of 77 out of 210 = 36.6 per cent.

The increased frequency of fibrinous pneumonia during the influenza period appears most prominently from the foregoing mortality list. We can look upon the fourteen cases during October as an average corresponding to the ordinary frequency of the pneumonia cases and then we find an increase of five to sixfold during the influenza period. In January the frequency sank to double and in February reached the normal figure once more. The male sex is somewhat more frequently attacked than the female in the proportion of 1.76 : 1, and the mortality is also greater in males.

Krannhals also made a table showing the morbidity at different ages. The age of the patients was stated in 181 cases:

Ages.	October.	November.	December.	January.	February.	Total.	Died.	Mortality, per cent.
1 to 9 years.	2	3	1	5	..	11	3	27.3
10 " 19 "	2	2	7	3	4	18	2	11.1
20 " 29 "	2	8	10	..	5	25	7	28.0
30 " 39 "	4	23	7	4	2	40	14	35.0
40 " 49 "	2	12	10	5	1	30	4	13.4
50 " 59 "	2	13	9	1	2	27	13	48.2
60 " 69 "	..	8	7	1	..	16	10	62.5
70 " 79 "	..	2	..	6	2	10	7	70.0
80 " 89 "	..	..	3	..	1	4	4	100.0

Those of middle age (20–50 years) are especially liable, yet there are many beyond 50, particularly in November and December. The mortality was irregular as regards both the individual months and the

ages. December shows the highest mortality figure (43.9 per cent.), and the greater number of old patients during this month is also noticeable. The relative mortality for the middle-aged (20–50) was 25.3 per cent. In those beyond 50 years of age the mortality rose to 48.2, 62.5, and 70 per cent. From the material of the state hospital Krannhals showed quite a similar increase, and these statistics are of considerable significance because in all of the cases the pneumonia was demonstrated as of the true lobar fibrinous form. The following is a tabular statement of the undoubtedly fibrinous pneumonias occurring during the influenza period. The table includes not only the patients entering the hospital with pneumonia, but those under treatment for other diseases in whom pneumonia developed subsequently.

	I. Admitted on account of pneumonia.	II. Intercurrent fibrinous pneumonia in other patients.	III. Total.	Fatal Cases.		
				I.	II.	III.
October	5	3	8	1	3	4
November	32	3	35	12	3	15
December	4	2	6	3	2	5
January	16	1	17	3	1	4
February	11	2	13	2	2	4
March	8	..	8	2	..	2

Krannhals has also reported the results of 32 autopsies performed by him at the state hospital upon cases of fibrinous pneumonia. Of these 21 were admitted with pneumonia; in 11 cases there was fibrinous pneumonia which complicated other diseases. In the majority of cases he also made bacteriological examinations. Pathologically all these were cases of typical fibrinous pneumonia. Most of them were in the stage of gray hepatization, but the lesions differed in no way from those of ordinary fibrinous pneumonia. On the whole Krannhals had the impression that the tendency to suppuration was greater in these cases than is usual in pneumonia, as regards both the process in the lung itself and also the complications of purulent pleurisy, pericarditis, and mediastinitis. The capsule cocci were found in the exudate of the alveoli of the lungs in all but two of the cases examined (seventeen). These appeared, by their peculiar staining, to be Fraenkel's cocci, and in eight cases were proven to be such by cultures on agar plates. In addition to the pneumococci there existed —as is always the case—a certain number of other microorganisms, mostly pyogenic cocci, and of these first in order streptococcus pyogenes. These pus cocci appear to have been mixed in greater numbers than I have generally found.

In a few cases they far outnumbered the pneumococci in the dry preparation as well as in the plates. As far as concerns the clinical course of the cases collected by Krannhals, it is distinctly stated that of the thirty-two cases upon which an autopsy was performed, nine showed a typical beginning and a typical course of the disease. In the other cases asthenia was very marked, and among these there were some in which a chill was not noticed at the beginning. In a third of the cases it was stated that influenza had preceded or that the pneumonia appeared as a complication during the course of influenza. Since nothing was said on this point, it is possible that in the other case there existed a genuine pneumonia without influenza. Of the 53 convalescent cases which Krannhals reports from the state hospital of Riga, 35 ended with crisis, 13 with lysis, and in 5 fever persisted until a radical operation was undertaken for a metapneumonic pleuroempyema. The results of Leichtenstern's studies of fibrinous pneumonia occurring during the influenza period agree in great measure with those of Krannhals. He mentions 76 cases of croupous pneumonia which occurred in the influenza period, but which on account of the imperfect influenza sputum had to be reckoned among the ordinary forms; and, among these cases it was worthy of note that an unusually large number was from the very beginning bilateral.

Frequently the lesion on one side was lobar from the first, while that on the other side remained lobular throughout. Most of these cases showed a very marked divergence anatomically from typical croupous pneumonia. Thus Leichtenstern describes a case in which he performed an autopsy nine days after the beginning of a bilateral lobar croupous pneumonia. Naturally he expected to see the lesion in an advanced stage of its development, and was greatly surprised to find a fresh brownish-red hepatization of both lower lobes, which upon microscopical examination gave the picture of fibrinous pneumonia with considerable hyperæmia. Leichtenstern also observed cases of acute croupous pneumonia with very rapid course. In three cases occurring in robust individuals, both lungs, with the exception of a few aërated regions in the anterior parts of the upper lobes, were totally infiltrated within a few days. In Cologne there were also observed cases of true croupous lobar pneumonia of very short duration, so that very typical cases of aborted pneumonia of one day's duration were seen. Pneumonia ephemera, biduana, triduana, quadriduana also occurred. In some cases of lobar infiltration the disease ran an extraordinarily long course. Krannhals asserts that the fibrinous pneumonias of the influenza period were no more frequently accompanied by complications

than the pneumonias of any other period, and he shows this by the following table:

Typical fibrinous pneumonias.	July 1, 1887, to June 30, 1888.	July 1, 1888, to June 30, 1889.	Influenza time.
Without complications	21	26	23
Complicated with empyema of the pleura	2	..	..
Complicated with purulent mediastinitis	1	..	..
Complicated with empyema of pleura and mediastinitis	..	..	3
Complicated with meningitis pneumonica	3	4	..
Complicated with endocarditis acuta	2	..	..
Complicated with endocarditis and meningitis	1	..	..
Complicated with pericarditis	..	1	3
Complicated with laryngitis crouposa	..	..	1
Complicated with phlegmon	..	..	(1)
Total	30	31	31

This interesting classification refers to the results of autopsies; it must still remain a question, however, whether clinically the complications were not more frequent than the foregoing table would seem to indicate. Meningitis and pleuritic affections have also been described as complications of fibrinous pneumonia. Of 220 cases occurring in private practice in Riga, pleuritis exudativa was noted in 12. Among 87 hospital cases, in 7 there existed a pleural exudation of considerable amount. Krannhals describes 2 cases of pneumonia with unusual course which he designated as erratic or recurrent pneumonia.

One case was that of a diabetic patient in whom, on the 28th of December, with a slight chill and sharp pains in the cardiac region a pleurisy developed. During the next few days there occurred a circumscribed exudation in that region; on January 10th, the exudation being not yet entirely absorbed, the patient had a chill and dry cough, but examination of the lungs was negative; on the following day, in the lower part of the left lung posteriorly, there was found a circumscribed consolidation, the sputa were rusty and contained large numbers of Fraenkel's diplococci; three days afterwards there was a fall of temperature, with slow clearing up of the area of dulness. On January 16th the temperature rose again; there was pain on the right side anteriorly, and during the next few days a large pleuritic exudation developed in this region; while this still remained, and the temperature began to fall, there developed on February 15th with a chill the physical signs of a pneumonia in the lower part of the right lung posteriorly. Rust-colored sputum with an abnormal quantity of diplococci, slow lysis, and death from exhaustion on March 16th.

The second case was that of a woman, 50 years of age, who, after a chill, was found to have a left-sided pneumonia marked by a

sharply circumscribed area of dulness, bronchial breathing, and rusty sputum. On the third day, there was a fall of temperature with profuse sweats. After three days the same symptoms were repeated, the dulness being somewhat higher this time. Five days after the second fall of temperature, there developed for the third and last time, in exactly the same manner, a right-sided pneumonia.

These cases remind us of those of Leichtenstern, who, under the name of pneumonia repetens or subsequens, describes cases of lobular or lobar pneumonia, which occurred successively in different parts of the lungs with apyretic intervals or remissions.

One of Leichtenstern's cases was that of a man, 21 years of age, who was taken ill with a typical influenza on December 24th. On December 26th there was entire absence of fever and complete euphoria. On December 28th there was a chill, followed by dyspnœa; the expectoration was bloody and purulent. In the right middle and left lower lobe, crepitation and relative dulness, temperature 40.6° (105°). On the 30th a crisis occurred with complete defervescence. On January 1st without a chill there was a rise of temperature to 40.3° (104.4°) accompanied with dyspnœa; examination showed a pneumonic area in the lower part of the left upper lobe. On January 4th complete apyrexia; on January 5th another chill, and a new area in the supraspinal part of the left upper lobe. On January 9th a fall of temperature occurred by crisis, and although there was now continued apyrexia, the purulent expectoration persisted for two or three weeks longer.

Another similar case is reported by Leichtenstern, and is to be considered as very unique, because the pneumonia repetens attacked the same lobe twice. The right upper lobe was the one thus attacked. The second attack occurred three days after the crisis of the first. The second pneumonia ended with crisis on the eighth day. We should, however, decidedly underestimate the infection of the lungs with the diplococcus of Fraenkel, which occurs in influenza, were we only to present cases running a typical course. These are very interesting, but they are by far the least frequent form of influenza pneumonia, the symptoms of the croupous pneumonia usually being greatly modified by those of the preexisting influenza. Notwithstanding the varied clinical picture, however, it was shown by the post-mortem and bacteriological examination that such atypical forms were true cases of croupous inflammation of the lung. The following are the various forms under which croupous pneumonia, as modified by influenza, appears:

1. The initial chill is frequently absent. It is either covered by the influenza symptoms such as repeated chilly sensations interrupted by sweats, or the temperature rises briskly without a chill. 2. Whereas in the genuine croupous pneumonia the skin remains dry

during the height of the fever, in the fibrinous pneumonias of influenza we see severe sweats, sometimes of a profuse character, without any fall in the temperature. 3. The disease terminates less frequently by crisis, more frequently by lysis, and while in primary pneumonia a feeling of well-being often exists immediately after the crisis, where the disease occurs with influenza there more frequently exist, after the fall of temperature, a marked weakness, persistently rapid respiration, and loss of appetite. 4. As of special interest are here to be mentioned the various forms of irregularity in the course of the fever which were previously described in speaking of lobar pneumonia. Remittent or intermittent pneumonia, the repeating forms of varied duration and occurring on various days, are noted in the lobular as well as in the lobar fibrinous pneumonias of influenza. Often the lesions in contiguous areas of the lung are in the most varied stages of development. The rusty sputum of a frank fibrinous pneumonia is often absent, and we must not exclude pneumonia from the failure of this symptom alone. I would insist here upon a point of special importance in the diagnosis of pneumonia in influenza. In many cases the only physical sign pointing to a pneumonia was the presence of small areas of dulness on percussion, there having been absolutely no crepitant râles audible in the beginning, but the diagnosis was later confirmed by the appearance of a râle redux upon the setting in of resolution.

We may assume to-day that the vast majority of cases of fibrinous pneumonia are caused by the diplococcus of Fraenkel. It should be remembered here that this diplococcus may give rise to both lobar and lobular pneumonias of a fibrinous nature. Netter has tabulated the results obtained in 121 autopsies and 31 clinical cases. In 82 adults there were 103 instances of diplococcus infection. Among these were 54 lobar pneumonias = 65.95 per cent. of the individuals; 13 bronchopneumonias = 15.85 per cent. of the individuals; 1 capillary bronchitis. In the 54 cases of pneumonia it could be assumed that the condition was primary, and the 13 cases of bronchopneumonia also showed the primary symptoms of the diplococcus infection.

Cellular Pneumonia.

We have described the pneumonia caused by the influenza bacillus of Pfeiffer, which is a bronchopneumonia; then the fibrinous varieties, both lobar and lobular, due to the presence of Fraenkel's diplococcus, and there now remains a group of pulmonary inflammations, met with in the course of influenza, which histologically are pure cellular pneumonias. In the first group are the acute lobar cel-

lular infiltrations which Leichtenstern has treated of most exhaustively. "We have to note," he says, "a rare but clinically important form of pneumonia which belongs to the group of cellular inflammations and which is usually therefore classed with catarrh but which really deserves a place by itself." He thinks this is the same form as that encountered in the course of scarlet fever, whooping-cough, measles, etc., and therefore in no sense peculiar to influenza. It begins very often quite acutely, after the manner of a croupous pneumonia, invading at one bound an entire lobe, more commonly an upper lobe, and not infrequently is mistaken for croupous lobar pneumonia, its true nature not being recognized until the case comes to the autopsy table. The cut surface of the lung is perfectly smooth, homogeneous, of a light red to a purple color, shining, of hard, elastic, fleshy consistence, containing no air whatever. On pressure it is impossible to express any fluid or air, nor do any drops of pus exude from the cut ends of the bronchial tubes. Leichtenstern is firmly of the opinion that this acutely beginning lobar infiltration does not arise from the fusion of lobular foci nor after the manner of an ordinary bronchopneumonia, belonging neither clinically nor anatomically to the latter.

Histologically this form of pneumonia is characterized by great hyperæmia, the alveolar septa are thick and infiltrated with round cells, the alveoli themselves being packed with cells among which are only traces of fibrin. The cells are in smaller number red blood cells, in greater number leucocytes, but most numerous of all are large squamous cells which are to be regarded as swollen and cast-off alveolar epithelial cells. Through this is differentiated, in a purely histological sense, this form of cellular pneumonia from ordinary catarrhal pneumonia which goes on to suppuration in consequence of a massing of leucocytes. Clinically and anatomically this is the same affection as that formerly incorrectly called the acute lobar desquamation-pneumonia of Buhl. Leichtenstern formerly designated the fleshy consistence of the infiltrated lobe by the term inflammatory carnification, but withdrew this term after Weichselbaum and Kundra applied the same name to something entirely different, namely, chronic induration processes. Leichtenstern asserts that rusty sputa are never seen in cellular pneumonia, by which fact alone, and by it only, the diagnosis from croupous pneumonia can be made with certainty. It has nothing whatever to do, he says, with the so-called primary streptococcus pneumonia, although many different cocci may be found on bacteriological examination, especially, as is so often the case in all forms of inflammation, streptococci. The presence of the influenza bacillus in this form of pneumonia is also noted.

Streptococcus Pneumonia.

Although the etiology of this disease has not yet been clearly determined, we find that there is also a group of cellular forms of pulmonary inflammation which must be referred to the action of streptococci. In the pandemic of 1889–90 cases were observed, in many different places, of a combination of influenza infection with streptococcal invasion, and especially in Bonn were extensive studies made of this form of disease. From an examination of the literature we can see that during the influenza period mention is made much more frequently of the presence of streptococci in the inflamed portion of the lungs than of Fraenkel's diplococci. At this time I discovered and accurately described streptococcus pneumonia, a primary cellular streptococcus infection. As soon as the streptococci invade the parts occupied by the influenza bacillus they excite this peculiar inflammation of the lungs. As this process is of a cellular nature and presents none of the characters of a fibrinous inflammation, so we find the symptoms of streptococcus with influenza-bacillus infection accompanied by pulmonary symptoms recalling a picture of a pure streptoccocus infection. We shall first describe primary streptococcus infection of the lungs, and then the combination of this with influenza.

In the year 1887 I observed a series of six cases, belonging to the group of cellular pneumonias, which ran an extraordinarily pernicious course. In every case there were all the evidences of a profound intoxication, and in three death occurred. Two years later I saw two other cases in a lad and his father. Then during the influenza epidemic of 1889–90 I encountered a long series of similar cases, and six more in 1890 after the epidemic had died out. In 1891 I saw three, of which two ended fatally. In the winter of 1893–94 I saw five cases, two of them in patients in the hospital under treatment for other diseases; these differed essentially, by reason of their wholly benign course, from the cases I had previously seen.

A woman, 28 years old, entered the hospital on December 24th, 1893, with a history of a sudden seizure with headache, sore throat, and chills three weeks before, and sharp pain in the left side one week before. Percussion gave dulness over a wide area on the left side below over approximately the lower half of this lobe. Auscultation revealed bronchial breathing with very fine crepitant râles; the respiration was rapid, the pulse was small and weak, and a deep inspiration caused pain. The temperature was not elevated—most of the time, indeed, it was subnormal. During the next four days the dulness diminished, the râles became moister, and expectoration was more profuse; ten days later there was no dulness, but crepitant râles

were still audible. Four weeks after admission the patient was discharged cured. As influenza prevailed at the time it was thought this might be a grippal pneumonia, but examination of the sputa revealed only streptococci and neither diplococci nor influenza bacilli. On January 17th, when the expectoration had already become very scanty, no more streptococci could be discovered, but only a few short, thick bacilli arranged in chains or aggregated in masses.

On January 15th, 1894, a patient, 34 years of age, who had been in the hospital nearly three years with chronic myelitis, was seized with spasmodic pains in the back and legs, headache, general malaise, and a feeling of exhaustion. On January 18th it was ascertained that he had had several chills during the night, and an examination of the chest revealed dulness and crepitant râles over the right upper lobe both in front and behind; the respiratory murmur was weakened here, but throughout the rest of the thorax the physical signs were absolutely normal. There was little cough, and expectoration was wholly absent the first day. On the third day of the disease the process invaded the right lower lobe posteriorly, the left lung still remaining free; at the same time there was a scanty, thick, yellow, purulent expectoration. On the fifth day there was fine crepitation over the right middle lobe, and the patient was visibly weaker. The following night there was a profuse sweat, accompanied by cyanosis, and the pulse rose to 120. The consolidated areas remained relatively about the same until the beginning of February, when numerous crepitant and subcrepitant râles became audible and the lungs cleared up perfectly. Up to the middle of this month, however, night sweats occurred repeatedly and reduced the patient's strength alarmingly. From the 15th to the 21st of January the temperature rose gradually to 39.7° C. (103.5° F.), and then gradually sank to normal during the following six days and there remained. From the third day of the disease, when expectoration first appeared, to the middle of February the sputa were regularly examined bacteriologically. The very first microscopical examination showed the presence of streptococci in large numbers, and agar cultures gave streptococci only. No influenza bacilli could be seen under the microscope, nor could they be discovered in cultures grown on media specially prepared with pigeon's blood. For a few days during the course of the disease a few staphylococci were found in cultures but they disappeared later, pure cultures of streptococci only being obtained during the later period of the pneumonia.

Three other cases of the same sort were observed, two in hospital and one outside in an entirely different quarter of the city. In all, examination of the sputa showed the presence of streptococci only.

We are forced to admit, therefore, that inflammation of the lungs as of the bronchi may be excited by streptococci. The inflammation is of a cellular, not a croupous, character, and lobular, not lobar. In all my cases it was found, either clinically or on the post-mortem table, that there were multiple areas of consolidation, although some-

times many small ones had eventually run together to form one of some size. It is seldom, however, that the infiltration is pseudo-lobar in extent, for usually portions at least of the affected lobe remain free.

To the naked eye the lesions show changes in color and consistence. They are seen on the cut surface as reddish patches, with irregular, jagged contour, dotted here and there with grayish points and splashes. The bronchial tubes are open or only here and there occluded. Under the microscope these areas are seen to be lobular in extent and having the character of an acute interstitial pneumonia with loose exudation in the alveoli, chiefly of a catarrhal nature and with only an occasional admixture of fibrin. The alveoli are filled with fluid containing large and small squamous and round cells. An increase in connective tissue is seen round the vessels and bronchi.

As regards the cure of the disease, I have shown in previous articles that we may have actual epidemics of pernicious cases; again, as in the cases detailed above, the disease may be of a benign character, or finally it may run a subacute or actually chronic course.

Acute pernicious streptococcus pneumonia may resemble typhoid fever or septicæmia; some cases have actually been mistaken for typhoid fever without intestinal symptoms. These acute cases vary greatly, as we have seen, as regards prognosis. In some cases, notably those occurring in 1893–94, the resemblance of the symptoms and course to those of influenza was most striking. We shall return to this resemblance later.

The subacute and chronic cases are especially interesting in that they offer a very striking similarity to pulmonary tuberculosis. We can readily understand this when we consider the physical signs of the two affections, but there is also a close resemblance in the general symptoms. The irregular and usually not very elevated temperature curve, the weakness of the heart and rapidity of the pulse, the frequent night sweats, the marked disturbances of nutrition, all these render the differential diagnosis so uncertain that we are able to determine this point only by an examination of the sputa or by an injection of tuberculin. Three years ago I had a patient with acute streptococcus pneumonia. I had followed the disease from the start and always in repeated examinations of the sputa, and once of the pulmonary infiltration itself through an exploratory puncture, had found only streptococci, never tubercle bacilli. After the acute stage had passed cough and expectoration persisted for a long time, and retraction of the chest took place on the affected side. Those of my colleagues who were familiar with this case were always doubtful of my diagnosis, but eventually perfect recovery ensued and the retrac-

tion, which had lasted for months, disappeared completely. I have also treated other cases of the same kind, some of which had been diagnosed as tuberculous, and the patients were naturally overjoyed to learn that their disease was not consumption. In these cases excellent results have been obtained by the use of guaiacol or creosote.

Wassermann has also described cases of streptococcus infection of the lungs in which, however, the severe acute general symptoms were entirely wanting and the prognosis was good throughout; these ran a subacute or chronic course and sometimes assumed exactly the picture of a tuberculosis. In all of Wassermann's cases the patients had been sent to him under the belief that they were tuberculous. The disease began with purely subjective symptoms, a distaste for work, and an actual inability to perform the ordinary daily tasks, alternating sensations of heat and cold, pain in the chest, cough, and often night sweats; at the same time there was a notable falling-off in flesh. The localization of the disease varied, but it was usually found at the apices. The signs elicited by percussion and auscultation were very similar to those obtained in tuberculosis. The temperature was somewhat peculiar and was characterized by an excessive irregularity, rising suddenly at any time of day, often with a chill and frequently without, remaining at a greater or less elevation for an altogether indefinite period but always with sharp oscillations, and falling again unexpectedly, showing the jagged and peaked outline of the streptococcus temperature-curve.

The character of the expectoration is especially worthy of note. In some cases there is quite a profuse expectoration, pointing to a participation of the bronchial tubes in the inflammatory process or to the existence of a pulmonary abscess; on the other hand, cases occur in which the expectoration is slight or wholly absent. The latter is the condition, according to both Wassermann's experience and my own, in the majority of cases, and when there is no expectoration whatever our only means of making an absolutely certain diagnosis is wanting. This fact argues strongly in support of my contention from the first that we have to do here with an immediate primary disease of the pulmonary tissue itself caused by the infectious agent, with that sort of a disease which has led me to describe streptococcus pneumonia as a cellular pneumonia. This cellular character of the anatomical changes it is which explains their persistence, and also the fact that they seldom disappear without leaving cicatricial tissue behind; the lesion is not a superficial one, like that of fibrinous pneumonia, but is an interstitial one.

If we are compelled to establish a differential diagnosis from the physical signs alone, we shall be aided by remembering that in strep-

tococcus infection, more often than in tuberculosis, extensive portions of the lung substance will be found in the same condition. Also I find more frequently in streptococcus infection crepitant, not sonorous, râles over extensive areas, while the dulness is less pronounced than in tuberculosis.

It has been said above that cases of acute streptococcus infection as well as the acute exacerbations of the chronic form often bear an astonishing resemblance to influenza. Some of the cases occurred in the midst of an influenza epidemic and were at first supposed actually to be cases of influenza. Now that we are fortunately able to recognize pulmonary influenza with certainty by the discovery of the specific microorganisms in the sputum, those cases of streptococcus pneumonia are shown to be such by the discovery of streptococci in the sputum and the repeated failure to detect influenza bacilli in the same. Reasoning from my present experience, I have no doubt that very many of these streptococcal inflammations occurring during the winter of 1889–90 were incorrectly diagnosed as grippal pneumonia. This would smooth away many apparent contradictions; it would explain the curious fact that in some places large numbers of streptococci were found in nearly every case examined bacteriologically, while in other cities or other hospitals in the same city diplococci were found to be the active agents in the causation of the disease.

The difficulty of differentiating streptococcal inflammation of the lungs from grippal pneumonia is greatly increased by the fact that not only the physical symptoms but also the lesions may be the same in the true affections, and we are therefore thrown back on a bacteriological diagnosis.

Grippal pneumonia arises most frequently in consequence of an entrance of the influenza bacillus into the alveoli through the bronchi. Whether the same may occur in the case of streptococcal pneumonia we cannot say, but we know that this is not always the mode of entrance of the causal microorganism.

Streptococcal pneumonia is proven by the facts of its occurrence to be contagious. Whether influenza prepares the soil for the streptococcus or whether there is some other reason, it is a fact that streptococcal pneumonia is more common during an epidemic of influenza than at other times. In my first cases the course of the disease was most malignant in character, but later I saw many which ran a very mild course, and Wassermann also found that streptococcal pneumonia was benign in character. Thus it appears that the gravity of the disease varies greatly in different epidemics, due no doubt to the varying degree of virulence of the streptococci.

It may be asked on what grounds I base my belief that the cases

occurring in Bonn during the influenza epidemic of 1889–90 were actually cases of streptococcal pneumonia and that there was not an accidental contamination with streptococci. But we might also argue that we had no grippal pneumonia at all, but that all the cases of pneumonia were streptococcal. The influenza bacillus had not been discovered at that time. I am quite certain, however, that at least in Bonn there was a mixture of streptococcal and grippal infection, that in fact we had a true epidemic mixed infection. In two of my cases it was shown unmistakably that pure streptococcal inflammation of the lungs may occur in the midst of an influenza epidemic, but it cannot be possible that all the cases occurring in Bonn in 1889–90 were only of streptococcal infection and not influenza; and I am even less inclined to admit this possibility since I had under my eye in some cases what were probably influenza bacilli. Pfeiffer writes in his work on the etiology of influenza that smear cultures made from the secretion covering the mucous membrane of the larynx and trachea usually showed a mixture of various bacteria, streptococci, Fraenkel's diplococci, etc., but that very regularly among them were found the influenza bacilli in far the greatest number. In the bronchi the admixture with other bacteria became less and less noticeable, and in the purulent contents of the finer bronchial twigs, as also in the pulmonary substance, the influenza bacilli alone were found. I can confirm this statement by the results of my latest investigations, and precisely for that reason do I maintain that the streptococci which I obtained from the pneumonic areas through exploratory puncture, often in the very earliest stage of the local pulmonary inflammation, are not to be looked upon as accidental intruders of no significance as regards the character of the inflammation, especially not when, as in nearly all the cases, only streptococci, and no diplococci or other ordinary bronchial bacteria, were found.

Since the publication of Pfeiffer's discovery I have examined again all my preparations of the streptococcus pneumonias occurring during the course of the influenza epidemic. I find in them the same condition in the bronchi, the collections of pus, the raising up of the epithelium, the thickenng of the wall, while in other bronchi no changes whatever had taken place. In the pulmonary tissues there were thickening, increase of connective tissue, an increase in the width of the septa, an infiltration with round cells, and in many alveoli an exudate poor in fibrin but rich in cells, as in pure influenza. But the stain which I used at that time was not suited to the differentiation of influenza bacilli.

As stated above, I am convinced of the contagiousness of streptococcus pneumonia. In my first series there fell ill a mother, then the

son, then a female relative who was acting as nurse, a male nurse, a nursing sister, and the clergyman who had visited the latter; in the second series were a father and son; in the third, a man and his wife and the physician who had attended them. The many cases which I saw in the first influenza epidemic often occurred in groups; for example, there were four severe cases on a farm in the persons of a mother, her daughter, her son, and the wife of the latter; the daughter died, the others recovered after a long illness. Many took sick in the hospital after other patients had been admitted. It may be asserted that the influenza was the actual basal disease in these cases, but in that case the streptococcus infection must have been added to it. The streptococcus disease must therefore be contagious.

Peculiar Forms of Pneumonia.

Between the pneumonias, hitherto discussed, it is possible to trace a certain etiological relation as a basis of classification. Thus the group of pneumonias produced only by the presence of the influenza bacillus is self-evident, also that produced by the diplococcus pneumoniæ, and finally the complication of influenza with streptococcus pneumonia. This does not, however, exhaust the various forms of pulmonary inflammation occurring in influenza. There are other pulmonary diseases, which are mentioned by some authors as peculiar forms of influenza pneumonia, which should, however, probably be more correctly looked upon as mixed infections, leaving undecided whether they have originated as mixed infections in the beginning, or whether the foreign bacilli have only been added to the influenza bacilli in the course of the disease.

Septic and putrid pneumonias, gangrene of the lungs, suppurative pneumonias, abscess of the lungs, have been frequently observed. The frequent occurrence of circumscribed pneumonias, which ended in abscess, was in a high degree noticeable during the epidemic of influenza. We must differentiate between two groups of the affections, viz.: (1) putrid pneumonia and gangrene of the lung, originating either idiopathically or added to a purulent bronchitis, bronchiectasis, and similar grave affections which had previously existed; and (2) septicopyæmic affections which complicate a primary deposit of pus in some other portion of the body. A case of this kind has been minutely described by Krannhals, which resembled both in its course and the findings at the autopsy Finkler's streptococcus pneumonia, in which, however, the streptococci were not found.

A man, aged 35 years, formerly syphilitic, was taken with a chill on January 16th, 1890. There were distinct symptoms of influenza, temperature 38.5° (101.3°), no objective symptoms. On January

18th, stabbing pains on the left side, below the arch of the ribs, came on; over the left lung were disseminated, large and small bubbling râles. During the following days the catarrhal symptoms increased and there was complete insomnia. On the 22d, the catarrh was also noticed on the right side, and slight icterus occurred. On January 23d, dulness in the lower part of the left side posteriorly was marked, also beginning in the lower part of the right chest posteriorly. The weakness increased, and on January 26th the patient died. At the autopsy both lungs presented changes, more advanced on the left side; the lower lobe was voluminous as in fibroid pneumonia, firm, very brittle, easily broken by pressure; on section the surface was seen to be dark gray, nearly smooth, presenting only the slightest indication of granular substance; it was thickly dotted and crossed in all directions by yellowish streaks in which the substance of the lung was of nearly fluid consistence. On closer observation it was seen that the seemingly diffuse lesions of both lower lobes were due to the confluence of numerous individual pneumonic foci, whose central portions had a yellowish, softened appearance, and whose periphery was gray; with this were present small, sharply defined abscesses, filled with a brownish, fetid pus. The pulmonary pleura presented a slight fibrous, puriform deposit and about 200 c.c. of a dark yellow, turbid, bad-smelling serum. A bacteriological examination revealed cocci, which were not the ordinary pus microbes, and bacilli of extraordinarily small size.

In another case which ended fatally with severe cerebral symptoms an area of consolidation, the size of an apple, in whose vicinity the pleura showed whitish, necrotic discolorations, was found in the lower lobe of the right lung, occupying the free border laterally. On section the whole deposit was found to consist in a great number of confluent, broken-down cavities, filled with a grayish-green fetid pus. In the pleural cavity was found a fetid seropurulent exudation to the amount of 1,500 c.c. There were highly fibrinous purulent deposits, but nothing else. Bacteriologically there were found mainly staphylococci, as well as the rod-shaped bacteria which liquefy gelatin.

The second group of Krannhals contains purulent but not putrid pneumonias: (1) Acute abscess of the lungs, without or with slight pneumonic changes; (2) secondary abscess of the lungs (complicating typhoid fever); (3) circumscribed non-fibrinous pneumonias going on to abscess formation; (4) abscess of the lungs, the result of a previous typical fibroid pneumonia going on to diffuse induration. Acute abscess of the lungs and circumscribed pneumonia eventuating in abscess formation are to be looked upon as especially characteristic of the influenza period, particularly if they occur in otherwise strong and previously healthy individuals. As an example the following case may be mentioned:

A girl, 18 years of age, a strong workwoman, who had formerly

always been healthy, was admitted December 3d. She had been taken ill ten days before with pain in the side, fever, dyspnœa; no bloody or rust-colored sputum. Diagnosis: Pneumonia fibrinosa sinistra, pneumothorax. Aspiration of the chest removed 2,100 c.c. of a thin pus, somewhat tinged with blood. The patient died on December 6th. At the autopsy, evidences were found of a slight serous mediastinitis; the left pleural cavity contained air and purulent serum. Both pleural surfaces were thickly covered with fibrinous purulent deposits. The lung was compressed, carnified. The lower lobe contained posteriorly and laterally an area, the size of a fist, consisting of a number of small abscesses containing a greenish, non-fetid pus. The largest, of the size of a walnut, was situated very superficially immediately below the pulmonary pleura, which presented at this point a whitish necrotic discoloration, and was perforated. The lung tissue situated between the abscesses was relaxed, not really consolidated as in pneumonia; there was no fibrinous pneumonia. On the right side also both pleural surfaces were covered with fibrinous deposits. The larynx and trachea contained bloody mucus, the mucous membrane of the bronchi showed dark brown areas of injection. The pus from the abscess contained diplococci and long cocci chains, the exudate on the pleura sparse micrococci, all being nearly without exception streptococci.

A second case is similar to this one. In the middle of November influenza was contracted; in the beginning of December dyspnœa and cough appeared, the mind became clouded, there was cyanosis, no expectoration was present; there was a bilateral pleuritic exudation, and both wrists were painful to pressure and on movement. At the post-mortem examination a pleuritic exudate of a dark-brown color and very turbid, and fibropurulent deposits were found; the left lung was compressed, containing no air; the centre of the lower lobe revealed an abscess the size of a cherry, filled with a dark-greenish-gray pus; there was no consolidation of the lung tissue in its vicinity; the left wrist-joint contained a few drops of greenish pus. The pus found in the pulmonary abscess, and the wrist-joint contained a great number of streptococci. We may probably take for granted in both cases that a circumscribed pneumonia had preceded the formation of the abscess.

Similar cases have been frequently described, in which was found a single circumscribed pneumonic deposit, situated on the border of a lobe of the lung, going on to abscess formation with a cellular alveolar exudation, and in which the greatest probability existed that the affection had resulted from a catarrhal peripleuritis, in which streptococci and staphylococci were present.

When in other cases the pulmonary abscess has developed after a fibrinous pneumonia had passed into diffuse induration, we may assume that suppuration has been caused either directly by the influenza bacillus, or by a mixed infection which was induced by the influenza.

The frequency of the formation of abscess and gangrene at the termination of an influenza pneumonia has been substantiated in literature by a great many observations. Pfeiffer and Weichselbaum noticed in influenza an accumulation of round cells in many small portions of the lungs in the peribronchial and interalveolar connective tissue, combined with necrosis and suppuration. They regarded these lesions as very small abscesses; thus, the formation of large abscesses, which have been designated as purulent pneumonias, is also intelligible. Ribbert and Marchand emphasize the inclination of the pneumonias of influenza to necrotic changes and the formation of abscesses; Zenker and Rhyner have observed abscesses and gangrene of the lungs, following fibrinous pneumonia due to influenza. Leichtenstern mentions five cases of abscess and two of gangrene of the lung following grippal pneumonia, and even at that time laid stress on the surprising fact that every one of these seven cases occurred in young and previously healthy persons. Hitzig in one case found the specific influenza bacilli in the pus of an abscess.

As regards the symptoms which are thereby caused, we must bear in mind all the changes which are usually found in gangrene and abscess formation of the lung. The grave febrile course of the disease, the periodical evacuation of large quantities of pus, the intercurrent hemorrhages which are at times very profuse, and the advent of pneumothorax, are symptoms which are not characteristic of influenza. In two cases reported by Leichtenstern a unilateral pneumothorax suddenly appeared in strong, youthful individuals at the height of the influenza process, accompanied by severe spasmodic cough. The autopsy in one case showed that no inflammatory process or abscess was present in the lung. The compressed lung on being inflated did not reveal the point of rupture, so that Leichtenstern took for granted in these cases that the violent paroxysms of cough had in the first instance caused a vesicular or subpleural emphysema, probably under the favoring influence of the pulmonary hyperæmia, and that the pneumothorax had taken place through the rupture of an emphysema vesicle, an occurrence which Leichtenstern compares to the similar changes which permit the passage of gas into the abdominal cavity through imperceptibly small injuries to the intestine.

Frequency of Pneumonia in Influenza.

From all that has been said of the pneumonias of influenza we may see that the diagnosis is in many cases very difficult. Some observers look upon even the smallest deposits in the lung as pneumonic; others again diagnose a pneumonia only when marked dulness

is present. This in itself is a sufficient reason for the great discrepancy in the number of cases of influenza pneumonia reported by different observers. Aside from this, however, we cannot doubt that in different localities, in other words, in different circumscribed epidemics, the number of cases of pneumonia complicating influenza varied greatly. Just as it may happen that in one city the diplococci preferably accompany the influenza, and cause all the symptoms of disease which are natural to them, and in other localities the streptococci accompany the influenza almost invariably, so there must have been localities in which mixed infections and their consequent pneumonias have made their appearance in varying form and in varying number. It is therefore hardly of any value to state an average number for the frequency of pneumonia, but it will be interesting to present some examples of the great disparity in the figures.

In the official report from Bavaria the statements from the different medical districts vary between 0.4 and 21 per cent. In Saxony the figures vary between 0.5 and 15 per cent. From these widely different figures then we obtain an average of 5 or 7 per cent. This figure is corroborated by the statistics of Litten, who met with from 6 to 8 per cent. on an average. The records from Switzerland gave for 3,230 cases of influenza, 93 cases of pneumonia, or 2.8 per cent. An extraordinarily low figure is given by Fleischer for Erlangen, namely, in 543 cases of influenza only 3 of pneumonia. Coler's figures for the Prussian army are also extraordinarily small, for out of 34,556 cases of influenza there were only 219 of pneumonia, or 0.6 per cent. In the statistics for the entire army he found 55,263 cases of influenza and 534 of pneumonia, or a little less than one 1 per cent. The statistics of hospitals give us a very much higher proportion of cases of pneumonia, for the reason, doubtless, that pneumonia patients especially seek admittance to the hospitals in times of influenza. In the City Hospital in Cologne, 24 per cent. is recorded; in the Hôtel Dieu at Paris, 22 per cent.; in Friedrichshain, 22 per cent.; in Hamburg, 17 per cent.; in Nuremberg, 12 per cent.; in Freiburg, 11.8 per cent. Lower figures are: In Riga, 4 per cent.; in Munich, 4 per cent.; in Leipsic, 4 per cent.; in Magdeburg, 3 per cent.

The mortality is greater in the pneumonia of influenza than in ordinary uncomplicated pneumonias. The German collective investigation placed the mortality at about 17 per cent. In the City Hospital in Cologne it was found to be 30 per cent.; in Riga, 43.9 per cent.; in Boston, 29.45 per cent.

Diseases of the Pleura.

We have gathered the information during the influenza epidemic that as a sequel to the pulmonary affection the pleura is frequently also involved, and as Pfeiffer found, in one case of influenza pneumonia, that the purulent deposit on the surface of the pleura was thoroughly saturated with influenza bacilli, the possibility of the causation of pleuritis by the influenza bacillus is thus demonstrated. On the other hand it cannot be doubted that a great number of the pleuritic affections occurring during the prevalence of influenza are produced by a mixed infection.

As to the frequency with which the pleura is affected we find that it occurs as a sequel in pneumonia, according to the tabulation of the collective investigation in Germany, in from 12 to 33 per cent. of the cases. If we examine into the frequency with which exudative pleuritis occurs, we meet with statements of some value in Krannhals, who found this infection of the pleura during influenza present in 12 cases out of 220; in 87 cases in the hospital an effusion in the pleura was present in 7, so this should not be looked upon as an insignificant complication. The exudation in these cases was as a general rule serofibrinous, but was purulent in 6 cases. A radical operation had to be performed in 5 cases, 3 of which recovered, and 2 ended in death on account of other organic affections. Krannhals is thus of the opinion that exudative pleuritis complicates inflammatory affections of the lung, during the existence of the influenza epidemic more frequently than at other times. We must of course bear in mind, in this conclusion, that just such cases attract attention to themselves in which the affection of the pleura plays an important rôle in the symptomatology of the disease. It is difficult to decide how frequently on the whole the pleura is involved in the pneumonic affection. Regarding this condition it has, however, been especially noted that during the prevalence of influenza severe pleuritic affections make their appearance. Krannhals has proved by figures the frequent occurrence of pleuritic affections, and a tabulation of the cases treated in the hospital at Riga during a number of years gives the following results:

Year.	Pleuritis serosa.	Pleuritis purulenta.	Total.	Year.	Pleuritis serosa.	Pleuritis purulenta.	Total.
1884...	17	14	31	1887..	18	15	33
1885...	15	25	40	1888..	26	21	47
1886...	20	20	40	1889..	32	39	71

The increase in the frequency of pleuritis has also been made evident on the post-mortem table, as shown by the following table of Krannhals:

Pleuritis serosa.	July 1, 1887, to June 30, 1888.	July 1, 1888, to June 30, 1889.	July 1, 1889, to June 30, 1890.
Idiopathic	1	3	6
In pneumonia	..	..	2
In tuberculosis	3	1	4
	4	4	12

Pleuritis purulenta.	July 1, 1887, to June 30, 1888.	July 1, 1888, to June 30, 1889.	July 1, 1889, to June 30, 1890.
Idiopathic	2	..	5
Metapneumonic	1	1	6
Septicopyæmic	3	1	4
In pulmonary abscess and gangrene	4	1	7
In tuberculosis	8	4	3
	18	7	25

The observations of this investigator have also shown that the number of cases of pleuritis, as far as they are taken from the hospital material, are divided in such a manner as to time that of seventy-one cases in the year 1889, twenty-nine, that is to say nearly one-half, occurred in the months of November and December. In the first half of the year 1890 a whole series of pleuritic emphysemas originating during the epidemic of influenza had to be operated on. Although one may at any rate hold the opinion regarding the purulent affections of the pleura which have occurred in the course of a pneumonia, that these secondary changes were not connected with the influenza, we are bound to regard the primary affections of the pleura, and especially the purulent forms, as being in close relationship with the influenza infection. A whole series of purulent emphysemas of the pleura has been observed without the occurrence of a lesion and without the presence of tuberculosis, in which a pulmonary affection could be demonstrated neither clinically nor anatomically, from which the pleuritis could have taken its origin. Very frequently it involved young and strong persons.

So far as the bacteriological findings of these cases of empyema are concerned, the streptococcus pyogenes is undoubtedly the most frequent cause. As it has been found in Bonn in purulent pleural exudates, so also has its continued presence been demonstrated by Krannhals in Riga in nineteen cases of primary empyema. In the metapneumonic empyemas the streptococcus is sometimes found alone, in

other cases, however, associated with the staphylococcus; in still other cases the staphylococcus is found alone. In cases in which the exudate existed contemporaneously with pulmonary abscesses Krannhals has also demonstrated the presence at times of the streptococcus and at other times of the staphylococcus albus and citreus. In one case in which a fibrinous pneumonia existed, he was able to demonstrate in the exudate the pneumococcus of Fraenkel, besides the streptococci. The pus-producing cocci therefore were found most frequently, and among these the streptococcus pyogenes plays the most prominent rôle. The observations of other investigators also prove that an affection of the pleura may follow, without the occurrence of a pneumonia, in the course of an influenza bronchitis. We must, however, note here that the pneumonic symptoms during influenza are of such a nature that they may be easily overlooked; Kundrat, Kahler, Weichselbaum, Netter, and Major have described a purulent pleuritis following the bronchitis of influenza.

Leichtenstern dwells with especial emphasis on the fact that there exists an extraordinarily grave, usually latent form of acute primary grippal pleuritis, which comes on nearly simultaneously with the attack of influenza, more frequently appearing on the second or third day of the attack; it sets in with a chill and a high, continued fever, leading at once to severe dyspnœa and cyanosis. In a short time rapidly increasing, not infrequently bilateral, deposits of most characteristic nature are formed. The fluid under these circumstances is turbid, seropurulent, of a peculiar dull-yellow color. Leichtenstern has demonstrated the fact in a number of sections that this pleuritis exudativa acutissima grippalis is a primary one, that is to say, leaving aside the grave diffuse bronchitis and the pulmonary hyperæmia, that it occurs without the presence of inflammatory infiltrations of the lung tissue. The exudate having the above-mentioned peculiar macroscopic qualities, produced bacteriologically a pure culture of enormous quantities of streptococci. Among the symptoms which are produced by the onset of this pleuritic affection, great dyspnœa is especially to be mentioned. After a bronchitis has come into existence, which in itself readily causes difficult breathing in influenza, the dyspnœa is increased in an astonishing manner by the intercurrence of the pleuritic affection, so that very strong, youthful individuals are sometimes suddenly taken off by this complication. As we are not able to find an explanation for this extreme dyspnœa in the mechanical changes alone, we have to deal here probably with an increased action of some poison.

Besides these exudative inflammatory forms of pleuritis, we also meet with a dry inflammatory process in this membrane, occasionally

even of an extraordinary extent, so that a friction sound can be heard over one whole side of the chest, and occasionally it may even be felt on palpation.

An extraordinarily stubborn course and a rapid loss of strength have in general been met with in the serofibrinous effusions occurring in the course of pneumonia. The purulent exudates, which occur during the course of a pneumonia, especially of the croupous variety, have usually exerted a deleterious influence on the organism. We are justified in assuming that the termination is fatal in the majority of cases in which these complications have been added to a pneumonia, and even in those cases in which the affection was cured by operation, it was followed as a rule by a very slow convalescence.

Many cases of retraction of the chest wall have been noted as the result of this form of empyema, and periostitis of the ribs is also mentioned as one of its not infrequent sequelæ.

Chronic Influenza.

When I assert that influenza may assume a chronic character, I do not refer to the fact that in consequence of the anatomical changes, which have perhaps taken place through the pneumonia of influenza in the lung tissue and in the bronchi, there gradually appear secondary conditions, such as catarrhs, contractions and their consequences. I refer here rather to the actual continuance of the influenza bacilli, and to a resulting chronic bronchitis or chronic pneumonia. Various authors, among them Pfeiffer, Wassermann, Beck, and Kruse, have assured us that the influenza bacilli may repeatedly be found in the sputum for weeks and months.

I have seen patients—and many a colleague will corroborate me from his own experience—in whom, after the influenza had passed away, cough and expectoration persisted; and without any known cause, at intervals of a few days or a few weeks, the catarrhal symptoms in the bronchi would return, so that again and again the cough and expectoration would be increased, and also frequently again decreased without any medical attendance. These are the cases also to which Kruse refers, which he found in Bonn, where he was in the position to follow individual cases for a long period of time, when he says that the influenza bacilli in truth continue to be found for a long time in large quantities and in pure cultures in the expectoration, but that the typical picture of the disease, in spite of the continuance of many of the symptoms, makes its appearance only temporarily or perhaps remains absent altogether. He was dealing here with patients who were affected with a chronic bronchitis or a small number

of foci of chronic pneumonia. Many of these cases only temporarily came under my observation, as walking cases, while I was able to follow others for weeks and months continuously until they were cured or died.

Just as in chronic phthisis, we also meet in chronic influenza with other bacteria. I have not met with any chronic bronchitic affection as yet which was due to a single variety of bacteria. It is nevertheless possible that a certain variety of bacteria occupy the foreground; it may be the stabile variety, which harbors as a guest periodically now one, now another microbic form.

Cases like this have been clinically traced and bacteriologically controlled for some time. The general health in these cases is extremely variable. At times the patients complain a great deal; at others they report joyfully their marked improvement. The deposits are, however, still present, even at the time of subjective well-being, and influenza bacilli are always found in the sputum. They may be at times sparse, at times covered by other bacteria. They may appear absent even on microscopical examination, and be plainly revealed only by the making of cultures, or they may not be coughed up at all for certain intervals of time.

In these chronic cases of influenza I am prepared for everything, whatever occurs in the acute form; sudden fever, neuralgia, attacks of perspiration of longer or shorter duration, digestive disturbances, asthmatic affections, coryza, anginas, all these make their appearance again without warning, alternating in such a manner that the patient often attributes the cause to the "change in the weather." In the same manner exactly, tabetic and asthmatic patients attribute their changing condition to atmospheric influences. Thus, for example, I was consulted by a man on February 7th, 1894, who was suffering with symptoms of influenza and of bronchitis with purulent expectoration. On February 15th, and again on February 20th, I found a pure culture of influenza bacilli in the sputa. Examination on April 3d showed numerous diplococci but no influenza bacilli, but on May 6th there were again great numbers of influenza bacilli. During this whole time the bronchitis continued, alternately improving and growing worse. In this case the chronic influenza was a continued infection, and although the intercurrent invasion of diplococci may perhaps have caused a temporary aggravation, the latter may happen without the appearance of other bacteria, and with simply an increase of influenza bacilli.

It must also be emphasized in this matter that a clear understanding of the case can be obtained only by a bacteriological examination, for I have also observed that very similar cases of chronic catarrh,

even those appearing as a sequel of influenza, may vacillate for years, and may also wander through different parts of the respiratory tract, ascending from the bronchi to the pharynx and nose, from here again descending to the capillary bronchioles; in these cases, however, the sputum does not contain influenza bacilli, but only diplococci. One is inclined to say that chronic influenza is a periodic affection which is subject to repeated exacerbations. Even when at times the influenza bacilli appear to be absent, they have probably not actually disappeared, but are hidden or have become few in number; they either need a certain time again to become virulent, or the individual has temporarily become immune, but again presents symptoms of the disease later on, after the period of immunity has passed. The latter is the most likely fact, for the reason that the symptoms of the disease are frequently absent, while great quantities of bacilli are met with.

Changes which are characterized by fibroid inflammation, consolidation, and connective-tissue formation in large areas of the lung tissue must be looked upon as lesions of a chronic form of influenza. These may cause very different kinds of symptoms. Occasionally this form of extensive pulmonary consolidation, which has occurred in one lobe or invaded an entire lung, is observed to consist obviously in a total interstitial change. The parts involved are in this case marked by an absolute flatness on percussion, this being at this time the only symptom of the existing change. The respiratory murmur may be decreased, all râles being absent, and yet this consolidation remains present, without any inflammatory bronchial symptoms for months and even years. These conditions may, however, also become complicated by the development in the area of consolidation of secondary purulent foci, or the formation of bronchiectases in which catarrhal symptoms of long duration have their seat. Two cases of this kind were observed by Leichtenstern, who had the opportunity to trace them without interruption from the acute attack of influenza to their lethal ending, which occurred two years later. He mentions that the question presented itself again and again at the patient's bedside whether he was not dealing with a case of tuberculosis, but he was continually persuaded by the total absence of tubercle bacilli to hold fast to the view that the chronic fibroid changes were due to inflammatory processes caused by the influenza. The autopsical findings corroborated this diagnosis to the fullest extent, a lesion identical in its gross appearance with certain fibroid forms of pulmonary tuberculosis was found, but the lung contained no tuberculous nodules. A microscopical examination still further demonstrated the absence of tuberculosis.

An observation belonging here was also made by Netter, who was

able in a case of pulmonary influenza, accompanied by great induration, to prove the presence of Pfeiffer's bacillus in the expectoration, with complete absence of the tubercle bacillus, for a period of fourteen months. Pfeiffer has also observed the presence of influenza bacilli in cases of chronic fibroid pneumonia. We should also, in these cases of induration, not lose sight of the possibility that other bacilli besides the influenza bacilli may be present. A special rôle seems to be played here by the streptococci, whose influence in the production of interstitial pulmonary processes has been demonstrated elsewhere in this article. The following is the report of a case belonging to this class, which ran its course under my own eyes at the hospital.

The case was that of a man, 90 years of age, who was living in the hospital as an old pensioner, and who contracted influenza there. He was taken ill January 27th, with marked symptoms of influenza; temperature 37.1° to 37.9° (98.8° to 100.2°); great dyspnœa; apex impulse of the heart imperceptible; pulse, 104; respiration was labored, 40 to the minute. On the right side dulness extended from the second rib downwards, the percussion note being somewhat tympanitic over the second rib. The abdominal muscles were very tense during expiration. The liver was tender on palpation and was pushed downwards, extending two finger-breadths below the border of the ribs. Anteriorly on the right side respiration was diminished throughout, but there was an absence of râles. Over the place where the tympanitic percussion note could be elicited, breath sounds, not bronchial in character, could be heard as well as some scattered very fine crepitant râles. On January 28th, the cardiac sounds were softened yet clear. Pectoral fremitus was diminished, but could still be felt. Complete dulness on percussion was obtained over the entire right lung, and in the same location bronchial breathing with loud bronchophony was audible. The temperature varied from normal to 38° C. (100.4° F.).

This condition on the right side remained unchanged for two months, without any expectoration whatever, without the slightest involvement of the bronchi, and without any fever. At this time an extraordinarily rapid failure of the bodily strength occurred, with complete senile dementia, so that the patient passed his fæces in bed, and did not recognize those about him. After the dulness had existed for two months, resolution took place in the right upper lobe in a very short time, without the appearance of râles, while in the lower portions the infiltration process remained unchanged. Repeated aspiration proved the absence of pleuritic fluid, and showed that we had to deal only with a firm consolidation of the right lower and middle lobes. In the early period, however, aspiration yielded a little fluid, in which streptococci were exclusively found.

The fact that influenza lasts in phthisical patients particularly an extraordinarily long period, that it becomes chronic in them, and

induces fresh inflammatory processes from time to time in the cicatrizing tuberculous areas, is of great interest. The following is an example of this condition:

A woman, 29 years of age, was suddenly taken in August, 1893, with cough and hoarseness, repeated chilliness and night sweats. The hoarseness improved but did not altogether disappear, the cough was also ameliorated, and expectoration became less. After six weeks all these symptoms suddenly increased again, and continued until the patient was admitted to the hospital. The woman was fairly well nourished, the thorax was flat with broad intercostal spaces, but the respiratory movements were ample. It was said that no tuberculosis had occurred in the family. Over the apices of both lungs the respiratory murmur, although not perhaps strong, did not indicate the presence of any changes. On the other hand there were dull areas over the liver anteriorly on the right side, and over the ninth rib posteriorly on the left side, and over these areas crepitation and diminished breath sounds were heard. This finding, the purulent condition of the sputum, and the previous history, aroused the suspicion that this might be a case of influenza, and examination of the sputum, in fact, showed an enormous quantity of influenza bacilli. The temperature remained normal, the pulse was somewhat rapid. After the inhalation of a solution of sodium chloride, and the internal exhibition of quinine, the hoarseness improved somewhat; the dulness in the lower part of the right side posteriorly disappeared about five weeks after the admission of the patient. But now there were evening exacerbations of temperature, headache, increased cough, more profuse expectoration, pain in the chest anteriorly over the upper part of the right lung, and in the same situation crepitant followed by subcrepitant râles. These physical signs progressed in the course of the next four weeks downwards anteriorly to the third rib, the sputum contained tubercle bacilli in small quantities as well as influenza bacilli. On January 11th, 1894, slight hæmoptysis occurred, and now the influenza bacilli were found to have disappeared, the picture of a right-sided apex tuberculosis only remaining; this had improved somewhat at the time of the patient's discharge, on February 6th, 1894.

The first affection, which made its appearance with the general symptoms described and presented local changes in the lower portion of the right lung, both anteriorly and posteriorly, and in the course of which influenza bacilli were found in the sputa, was undoubtedly influenza. This ran its course for a long period with slight symptoms, relapsing once, six weeks after its beginning. After the pulmonary changes belonging to it had improved, a tuberculosis of the right apex developed. I will not say in how far an influenza infection, which had existed for five months, was responsible for these last changes in the apex of the lung; but as a matter of fact the tuberculosis remained behind, and it is certainly possible that a be-

ginning tuberculosis was already present, though unrecognized, at the apex before the influenza began.

During the time in which influenza bacilli could be demonstrated, the temperature at first remained nearly normal for three weeks, and then presented a very irregular evening rise, scarcely exceeding 38° (100.4°), and more frequently half a degree Centigrade lower. Then occurred a period of about three weeks in which the temperature frequently reached 38.5° (101.3°) and once 39° (102.2°) in the evening; it then fell for two weeks to 37°–38° (98.6°–100.4°), again rising at one time to 39.9° (103.8°), but usually to 38.5°–38.8° (101.3°–101.8°), and at the end of our observations, after the tuberculous process in the right apex had begun to retrograde, the temperature became normal. The following is a highly interesting case:

The patient, a woman 26 years of age, had been admitted to the hospital in December, 1892, on account of a bilateral tuberculous affection of the apices, and a recent laryngitis. There were infiltration of both apices, cavities on the left side, and subacute inflammation of the mucous membrane of the larynx. The sputum was rich in tubercle bacilli. During one whole year the condition of the patient changed in such a manner that violent symptoms appeared from time to time, which were looked upon as an expression of the exacerbations, relapses, invasion of fresh territory, or whatever they may be called, which occur in chronic phthisis. Pleuritic inflammations repeatedly occurred, accompanied by acute pain, sometimes running their course with, at other times without an exudation. Such a pleuropneumonia of the left side made its appearance again on December 17th, 1893, accompanied by violent pain, fever, effusion, and an acute infiltration of the left lower lobe. This happened at the same time that cases of influenza were admitted in great numbers, some of these having already been in the hospital ten days. The patient was in a bad condition, the temperature frequently reached 38.3° (101°) at night, vomiting occasionally occurred, and diarrhœa added greatly to the patient's weakness. This attack passed off so that the patient was able to leave her bed again by the middle of January. As the sputa of many other patients were being examined, Dr. Kruse also made cultures from the sputum of this patient, and I was much surprised to learn from him that he had found influenza bacilli in it in large quantities on January 20th, on which day the patient felt very well. But the following morning, after passing a very bad night, she had a chill, and all the pains and miserable feelings complained of in her previous attacks returned again in full force; she was suffering from an attack of influenza. From this time on until June, the influenza bacilli were found; then again they were absent for about five weeks, to appear again subsequently. The patient became emaciated to a really extraordinary degree, there was œdema, and amyloid degeneration led to her death.

The observation that the influenza bacilli may remain seemingly

perfectly latent in patients suffering with phthisis and bronchitis, so that these patients become very dangerous carriers and disseminators of influenza, is of importance.

Thus I saw a patient in the hospital who had been admitted for tuberculosis of the larynx and of the lungs, and who died in a deplorable condition of this disease. During his life, Dr. Kruse as well as myself had repeatedly examined his sputum, finding great masses of tubercle bacilli, staphylococci, and streptococci. At the autopsy it was discovered that these two forms of bacteria were also present in the numerous foci in the lungs, while the contents of one cavity contained a pure culture of influenza bacilli.

I had the opportunity once of making a very careful observation in a case of tuberculosis of the lung complicated with influenza, from its beginning to the death of the patient, a period of eight months. The case was instructive in more than one respect. In the first place it illustrated how the influenza infection becomes the controlling force of the whole morbid process, inasmuch as the proof was found at the autopsy that not the tuberculosis but the advancing chronic influenza had caused the great destruction of lung tissue. The case was also of interest because, relying upon the results of tuberculin injections at an earlier period when little or no attention was paid to mixed infection, the entire course of the disease might have been ascribed to the tuberculous processes in the lung, while in fact it was proved that the progressive changes in the lung were in no manner caused by tuberculosis.

The patient, Lück by name, 21 years of age, was admitted to the hospital on July 20th, 1894, and died March 11th, 1895. Two hours after death the post-mortem and bacteriological examination was made. In the winter of 1893 he had had an attack of acute influenza, and after recovery from this, as it was supposed, he at times suffered from a severe cough, often accompanied by expectoration, and again not. In the spring of 1894 he felt much better, so that he returned to his occupation. In May, 1894, a severe cough troubled him again, although no cause for it could be found; the patient felt miserable, and was sent to the hospital by the physician of his benefit society. He complained of a violent cough, debility, and anorexia. The movements of the thorax were ample, but a deep inspiration caused cough. Over the left apex percussion was slightly modified; inspiration had a somewhat bronchial sound, expiration was sharp and prolonged, but there were no râles. Expectoration was very slight, but the sputum contained a large quantity of tubercle bacilli. Everything else was normal, the consolidated area in the left apex being the only lesion discoverable. On August 4th, the condition was the same. On August 11th, rhonchi were heard over the right apex, and also below the right clavicle, and influenza bacilli together with tubercle bacilli were found in the sputum. Notwithstanding

this the patient felt in general better. There was no elevation of temperature. Thus far I had made an attempt to treat the catarrhal conditions which were involving both right and left apices, but without success. My intention had been to wait until the complicating bacteria had disappeared before resorting to tuberculin injections. As I was not able to accomplish this, but as the patient nevertheless remained free from fever, I began the subcutaneous injection of tuberculin with an initial dose of 0.0001 gm. A general reaction did not occur, although increased inclination to cough, and increased râles over the apex of the left lung, and especially beneath the clavicle, were noted. Three days later this local reaction had passed away, and I made the second injection of 0.0002 gm. As this produced no constitutional disturbance, larger doses were now employed. After the third injection the general condition had greatly improved. The patient felt brighter, his appetite was better, his cough had diminished, and there was but little expectoration, so that I began to hope that this was the beginning of a lasting improvement. After the sixth injection, however, a marked change took place. The expectoration was materially increased, and the conclusion was reached that disintegration and the formation of cavities had begun. The cough also greatly increased, the general condition became worse, and the patient complained of great debility and pains in the limbs. The left apex showed distinct signs of a cavity, both anteriorly and posteriorly. Percussion over the right apex showed dulness, and many rhonchi could be heard below the clavicle even as far as the lower edge of the third rib. The sputum contained quantities of influenza bacilli, besides the tubercle bacilli. As I thought it likely that this change for the worse simply implied a very strong reaction, the injection of tuberculin was suspended for ten days, after which, the general condition having then improved, it was resumed, but the dose was not increased. The general condition again improved wonderfully and the examination of the sputum after the tenth injection revealed so few tubercle bacilli that it was difficult to discover them. On December 15th, however, four days after the eleventh injection, a marked change for the worse took place. Besides the processes going on in the two apices, numerous patches of pneumonia developed in the deeper portions of the lungs. The debility rapidly increased, and the pulse became still softer and weaker. The sputum contained only a few tubercle bacilli, but vast quantities of influenza bacilli.

As I had by this time reached the conclusion that the disease was not dominated by the tuberculosis but by the influenza, the tuberculin injections were discontinued. The pneumonic processes were now beyond control. They crept from one part to another, and caused an enormous retraction on the left side; the bodily weight rapidly diminished, the temperature began to rise, alternating with sweats, so that the picture of a septic process was presented. The strength now decreased, and death occurred from exhaustion.

The autopsy was made two hours after death. The left lung was reduced to a small volume, and contained air only at the extreme edge, and was permeated by fibrous bands, in which nodules were

embedded; the upper lobe contained cavities with fibrous walls; the lymphatic glands at the hilus were caseous. The right lung was totally adherent to the costal pleura, but contained more air; a few of the lymphatic glands were in a state of cheesy degeneration; the upper lobe contained a cavity of the size of an apple with fibrous walls; in the middle lobe there was a cavity the size of a walnut filled with pus, and there was another smaller one in its vicinity; the lower lobe was splenified. The bronchi exuded drops of pus. The lungs in fact presented all the lesions found in influenza, bronchitis, pneumonia, carnification, formation of abscesses, as Pfeiffer remarks, "a perfect pattern of morbid processes, illustrating the various changes in the pneumonia of grippe." In the sections it was easy to demonstrate the influenza bacilli in the bronchi, in the alveoli, in the cells, and in the tissues. As a rule the small bacilli in the interior of the cells were found grouped around the nucleus. Cultures made from the pus and deposits in various portions of the lungs contained in varying proportions influenza bacilli, diplococci, staphylococci, and large bacilli. Tubercle bacilli were not found in the left lung, but were pretty numerous in the upper portion of the right lung, where there was recent bronchitis.

After having studied this case I cannot rid myself of the thought that such mixed infections must have occurred also among the fatal cases of phthisis which we had treated by means of tuberculin in 1890-91. The question arises, whether it was not influenza which had caused the remarkably rapid aggravation of the symptoms observed in these cases of phthisis after tuberculin injections. That the administration of tuberculin was not the cause of the unfavorable course in these cases was shown by the fact that favorable results were obtained by the injection of tuberculin in another case, in which phthisis and influenza were combined, and also by the fact that in other cases in which tuberculosis was not complicated by a mixed infection, I have seen marked improvement result from the administration of tuberculin, and never even temporarily such a bad effect.

Diseases of the Digestive Apparatus.

The fact that, as already mentioned above, a division of influenza into respiratory, gastrointestinal, and nervous forms has been attempted, might easily awaken the thought that inflammatory affections, similar to those which have been described on the part of the respiratory apparatus, are also of frequent occurrence in the digestive tract. The facts, however, are in reality altogether different. The appearance of stomach troubles in different forms, the changes in the tongue and œsophagus, in many cases also the disturbance of the intestinal functions, are a part of the picture of influenza, but as a general rule a gastric form of influenza is mentioned only when the

symptoms on the part of the respiratory apparatus are slight. By this, however, I do not at all mean to convey the idea that these organs have remained in a normal condition. In the discussion of the diseases of the respiratory tract, attention has repeatedly been called to the fact that though only slight anatomical changes might be present in them, nevertheless we may have severe general symptoms. We are aware that when the influenza bacillus is present in the lungs or the bronchi, the most severe symptoms of poisoning show themselves in other organs; that this is also the case when the digestive tract is involved, seems to me to be highly probably.

The gastrointestinal symptoms of influenza are for the most part of a functional character, and it is only in the smallest number of cases that we find grave anatomical disturbances. For this reason the idea of the gastric form of influenza is rather a clinical than a pathologico-anatomical one. Thus it happens that physicians are inclined to take the view in cases in which the gastric symptoms are particularly prominent, that the seat of the disease is to be found here. The symptoms are usually those of a more or less acute indigestion. Most frequently the tongue is heavily coated, there is a bad taste in the mouth, the breath is foul, there is tenderness on pressure at the pit of the stomach, anorexia occurs occasionally, vomiting makes its appearance, and the action of the bowels becomes irregular. In one case constipation may occur, in another diarrhœa. All these may take place together, so that it is difficult to say whether the mouth, the stomach, or the intestine is chiefly affected, and these combine so strikingly with the general symptoms of influenza previously noted, *i.e.*, with the headache, the febrile movement, the aspect of the face, etc., that we are able from these symptoms to recognize the influenza as the primary disease.

If we follow the different sections of the digestive tract, we find *anorexia* especially mentioned in most descriptions, probably in three-fourths of the cases. This anorexia is frequently of long duration, while many different influenza localizations run their course; it often reaches into the period of convalescence, and is then the main cause for the retardation of recovery. The anorexia is frequently combined with an unpleasant taste in the mouth, which is often so pronounced that many patients complain of it without being questioned. Many patients have lost the sense of taste altogether, often the sense of smell also; others complain of an insipid, bitter, foul, or salty taste in the mouth. A disgust for food is particularly often met with. Accompanying this symptom the *tongue* is as a rule heavily coated. In many descriptions this coating is designated as characteristic, but it is difficult to assent to the statement that a peculiar tongue accompanies influenza,

in the sense that we are accustomed to speak of it in typhoid fever. The coating of the tongue is described at times as grayish-white, again as striped red or bluish-red, as fuliginous. Others again emphasize an intense even redness of the whole tongue, which is looked upon by them as an indication of an inflammatory change, glossitis. The changes of the mucous membranes of the mouth and the pharynx have been described above. The mottled appearance of the tongue is mentioned occasionally in the accounts of the disease by the older as well as more recent authors. Stomatitis simplex, vesiculosa, ulcerosa, were names given to various forms of this inflammation of the mucous membrane of the mouth. Hemorrhagic angina, hemorrhages from the gums, the back of the tongue, and the pharynx have been also described. Other authors mention tonsillitis and angina erythematosa as more or less frequent symptoms of influenza. These changes would of course in themselves suffice abundantly to explain the anorexia and the change in the sense of taste.

Following this we note gastric symptoms, among which *vomiting* is very frequent. In the German collective investigation this symptom was mentioned in 1,108 cards = 34.3 per cent. Among these cards were eleven in which it was specially stated that this symptom was always or nearly always present. Only one single card had the remark that vomiting was never present. This vomiting was described as being especially violent, at times intractable and lasting for days; and particularly in children, vomiting was frequently spoken of as being the only symptom. More severe symptoms, as hemorrhages from the stomach, were met with, but were by no means frequent. Although they happened so rarely, it is nevertheless quite important to be aware that an acute hemorrhagic gastritis may accompany an influenza, and that it may frequently be complicated with enteritis and peritonitis. The pathologico-anatomical findings have rarely demonstrated a severe affection of the stomach.

Jürgens lays particular emphasis on a few findings at the autopsy, in which grave ulcerative or hemorrhagic disease of the mucous membrane was present. He found broad but not deep ulcers, sometimes several centimetres in length, in the mucous membrane of the stomach, which was greatly swollen and intensely hyperæmic and œdematous; the mucosa and in part the submucosa were also œdematous and the seat of a cellular infiltration, as is the case in the beginning of a phlegmonous gastritis. While slight digestive disturbances were met with very frequently, according to many observers in nearly all the cases, these grave changes can have occurred only in a fraction, probably not so high as one-quarter of the cases.

Among the intestinal symptoms of influenza *diarrhœa* is most fre-

quently mentioned, and very commonly, indeed, is stated to have been the only symptom on the part of the digestive organs. We meet, however, with great differences in the statements of observers of the last epidemic, probably due to the fact that the disease acted differently in different places. Very frequently vomiting occurs at the same time with the diarrhœa, and we thus have the picture of a gastrointestinal affection, which in many cases runs an extraordinarily violent course. Thus Boese of Cologne has described a case in which gastroenteritis acutissima, appearing in the course of an influenza, simulated a severe attack of cholera, which nevertheless got well. Choleraic enteritis, convulsions, and coma were also observed by Holz in the case of two children in whom the symptoms appeared on the second day of the influenza. After an attack of coma lasting twenty-four hours, the children regained consciousness and finally recovered. Similar cases, in which the symptoms of cholera predominated or which reminded one of acute poisoning, are also described by Warfvinge. In the reports of the influenza epidemic in Bavaria, it is stated that alarming intestinal symptoms were frequently observed. The grave gastric forms were often preceded by attacks of cholera nostras, particularly in upper Bavaria, or dysenteric stools made their appearance, and even profuse but ephemeral intestinal hemorrhages were noted. From Würtemberg we learn that the gastric form alone occurred probably the most rarely of all, and mainly attacked children; even then it was a prominent form of the disease in only two circumscribed regions. As a rule anorexia, nausea, disgust for food, vomiting, and dyspepsia were the chief symptoms in the gastric form; stubborn intestinal catarrh, constipation or diarrhœa, and attacks of colic in the enteric form. Occasionally a catarrh of the large intestine with bloody stools and hemorrhage from the rectum occurred. In Baden it was also noted that the gastric form usually attacked young children and women, and then, as a rule, under the picture of a gastrointestinal catarrh. In a number of cases grave choleraic symptoms developed, and were even complicated with cramps in the calves of the legs. Of other symptoms which pointed to a severe involvement of the intestine were mentioned in the report from Baden the occurrence occasionally of a morbid picture resembling that of perityphlitis and peritonitis, accompanied by an obstinate singultus. In Hesse the involvement of the stomach and the intestinal canal was found to be a frequent accompaniment, and occasionally the affections of the digestive tract amounted to important complications and led to sequelæ which materially lengthened the period of convalesence. Symptoms of an acute gastrointestinal catarrh not infrequently preceded the other symptoms of influenza.

The suddenness of the attack, violent vomiting, repeated watery diarrhœa, cramps of the muscles of the legs, arms, and back, and cyanosis of the face simulated the picture of a severe case of cholera a number of times. In those cases in which the symptoms of the digestive organs were the most prominent, the anorexia, amounting even to an actual disgust for any kind of food, was most prominently mentioned.

Constipation, as a rule, was observed more rarely than diarrhœa. Frequently constipation was present from the beginning to the end of the disease; in other cases the alternation of diarrhœa with constipation was especially marked. Many of these cases of constipation can probably be explained without the presence of grave intestinal lesions; but there exists also a graver form of constipation, which is caused by a severe enteritis due to circulatory disturbances in the intestinal wall, which lead to paresis of the gut and meteorism. The great tenderness of the abdomen, the violent vomiting, and the collapse may in such a case simulate the picture of a general peritonitis, and the symptoms may reach such a degree of severity as to suggest the presence of an intestinal obstruction.

The fact is particularly to be noted that in some cases certain portions of the intestine become affected in a marked manner, under the influence of the influenza. The lower portion of the ileum and the cæcum become involved in a localization of a grippal enteritis with great pain in the vicinity of the cæcum, so that the picture of an appendicitis is presented. These cases have been described as typhlitis and perityphlitis caused by influenza (Teissier), and Leichtenstern believes that we are dealing here with a true inflammation of the cæcum without appendicitis. He observed during the pandemic of 1889 a few cases in which influenza and typhlitis were present at the same time, but he did not venture at that time to regard the two as having a direct causal relation to each other; he believed it to be a chance coincidence of influenza complicated with a common appendicitis. The later accumulation of such cases in literature, and his own autopsical experience convinced him afterwards of the existence of a grippal typhlitis.

A *typhoid form* of influenza has frequently been spoken of. If diarrhœa, distention of the abdomen, and catarrhal symptoms in the cæcal region are present, and the nervous symptoms of influenza are added, which may, as we know, increase from simple somnolence to a state of coma, or if meningeal irritation comes on, the picture of a case of typhoid fever may in truth be simulated to perfection. This likeness is still further increased if the tongue becomes dry, and if there is an exanthem which is either really roseola, or at least very much like it. The differential diagnosis may become still more diffi-

cult, as a marked enlargement of the spleen exists in both cases. The course of the disease in typhoid fever is, however, an altogether different one than in influenza, and the temperature curve especially will be for us the best guide to a correct diagnosis. Influenza begins also in most cases more abruptly than does typhoid fever, and the occurrence of a chill at the beginning of influenza will serve to distinguish this affection from typhoid fever.

The gastrointestinal symptoms occur not only at the height of the influenza, but also as sequelæ. In these cases the anorexia and accompanying gastric symptoms may last for weeks after the influenza has declined, so that a notable loss of flesh and even true *cachexia* may take place. Cases of this kind have been described in which the suspicion of cancer or of some other chronic affection of the stomach could not be dismissed. These grave cachexias, with marked loss of flesh, are, however, also often observed in those in whom there are only very insignificant anatomical changes of the stomach and intestinal canal. A marked decrease of bodily weight has frequently been observed. Leichtenstern visited a beer brewer, forty years of age, whose bodily weight decreased from 105 to 72 kgm. (231 to 158 lbs.) and whose aspect had become so changed that his friends were unable to recognize him. In the report of the German navy, Elste states that a marked loss in weight occurred in all cases, sometimes amounting to 11 kgm. (24 lbs.) in five days. Přibram made daily weighings of patients in his own family, and found a remarkable loss of weight, even during the very first days. From this we learn that the great loss of weight, in other words the grave disturbance of nutrition, is due not alone to the changes taking place in the stomach and intestinal canal. This is still further proven by the fact that marked loss of weight and of strength may also take place when the influenza has its seat in the respiratory organs, and no disturbances of any kind are present on the part of the digestive apparatus.

It is very strange that the gastric form of influenza does not always accompany the nervous and catarrhal form. Thus, more nervous and catarrhal cases were observed in the beginning of the epidemic in Berlin and elsewhere, and only later on the gastric forms increased. In other places the catarrhal cases, which were at first more frequent, gave way in the second half of the epidemic to the nervous forms; in other places again the neuralgic form prevailed in the beginning of the epidemic, then came the catarrhal, and lastly the gastric form. The collective investigation report has shown that the number of cases of slight digestive disturbances accompanying influenza was greatest in the northeastern part of Germany, while the severe and complicated forms prevailed in the southwest.

Following the affections of the stomach and the intestines, those of the *liver* must be mentioned. From a pathologico-anatomical point of view, there are observed in this organ hyperæmic conditions, parenchymatous degenerations, cloudy swelling, small-celled infiltrations, microscopic connective-tissue necrosis, and thrombotic formations. A grave form of liver disease, for example abscess of the liver, is probably to be looked upon as an exceedingly rare complication. Krannhals has reported four cases of this kind, in only one of which, however, a corroboration of the diagnosis was obtained at the post-mortem.

The first case was that of a man, 45 years of age, who was taken ill with influenza in December, 1889. Immediately after its beginning pain was experienced in the region of the liver; there was enlargement of the organ with tenderness on pressure, icterus was noted, and intermittent fever, particularly remarkable by reason of the intense chills accompanying it, occurred. Later, dulness was elicited over the lower part of the right side of the chest posteriorly, and an exploratory puncture demonstrated the presence of an empyema.

In the second case marked icterus occurred during the course of a bronchial catarrh shortly after the beginning of the attack of influenza; the icterus greatly increased, the spleen and liver were enlarged, chills made their appearance, and the patient succumbed.

In the third case the icterus occurred in the second week after the influenza had run its course; it was accompanied by tenderness on pressure below the right costal arch, and great enlargement of the liver, so that a distinct bulging of the right hypochondrium was observed. The fæces were colorless, the urine was strongly tinged with bile, and intermittent fever was present during the whole course of the disease. After a number of weeks, following a violent paroxysm of pain, the patient vomited blood, pus, and bile, and soon after the stools became bloody with a profuse admixture of bile, and the patient died.

F. S——, 37 years of age, was admitted to the City Hospital, February 4th, 1890. He had always been well previous to an attack of influenza, towards the end of December, 1889. This lasted three days and then recovery was apparently complete. From January 10th, 1890, two attacks of fever occurred daily, not accompanied by chills, but by perspiration. There were slight and infrequent pains in the right hypochondrium. There was also slight cough not accompanied by expectoration. The man presented the symptoms of a bilateral pleuritic effusion, with signs of consolidation of both lungs along the spinal column. The liver was not enlarged. The temperature rose during the daily attacks of fever to 40° (104°) and over. The effusion disappeared from the left side, and so also did the remaining symptoms of consolidation, while the exudate was increasing on the right side. On February 18th, exploratory puncture revealed the presence of a bloody fluid, in consequence of which aspiration,

which had been contemplated, was abandoned. The fluid, which was examined by me microscopically and by means of culture on agar plates, proved to be perfectly free from microorganisms. On February 21st, aspiration of the fluid became necessary to save life. Two litres (quarts) of a turbid, odorless serum were evacuated. The bacteriological examination revealed the presence only of the streptococcus pyogenes; pneumococci were not found. The effusion rapidly reappeared, and on February 22d the puncture was repeated. The fluid was now more purulent and slightly fetid. On February 24th, the patient died suddenly. At the autopsy the anterior mediastinal connective tissue was found saturated with a reddish, purulent serum, which had collected here and there in small cavities. There was no pericarditis. In the right pleural cavity there was found from 500 to 600 c.c. of a dark grayish-yellow, somewhat fetid pus; both pleuræ, with the exception of the diaphragmatic pleura, were thickly covered with a soft, fibropurulent exudate. The serosa was of a dark bluish-red tint and smoky. The right lung presented no lesion beyond a compression of the lower lobe. On the left side, perfectly normal conditions were present. There were soft adhesions between the capsule of the liver and the diaphragmatic peritoneum over the posterior portion of the convexity of the right lobe. At this portion cicatricial yellow spots gleamed through the liver serosa, and on section a group of small abscesses, filled with a greenish-gray pus, was found. The intervening substance of the liver was nearly liquefied. The boundaries of the abscesses were indistinctly defined, disappearing in a purulent infiltrated leathery substance. The rest of the liver was soft, and the lobules were unrecognizable.

Reynal described a case of pernicious jaundice following influenza, and others are reported to have observed an acute yellow atrophy of the liver during the course of an influenza. It seems curious that authors vary so greatly in the observation of icterus. In the older epidemics (1709, Lancisi; 1737, Huxham) a slight form of icterus is mentioned as an occasional symptom. Peacock draws attention to the fact that in the epidemic of 1847–48 there was generally present a certain icteric hue of the conjunctivæ or of the skin in general.

The reports of Bäumler in the last pandemic, who found so constantly a slight form of icterus that he regarded it as a diagnostically important symptom of influenza, are of especial interest. Of the male sex, 88.5 per cent., of the female, 76.8 per cent. were affected by this slight form of icterus of the sclera. This observation does not agree with that of Leichtenstern in Cologne. In 439 cases he observed icterus but twice during convalescence. The hospital statistics of Hamburg, Leipsic, Munich, Würzburg, and the English authors, Preston, Bristowe, and Parsons, do not mention the occurrence of icterus. In the German collective investigation icterus was reported in only 2 per cent. of cases. In Breslau, out of 234 physicians, only 4 mentioned the presence of icterus. Senator mentions

icterus only once, Comby met with it only once in 218 children, Weiss only 4 times in 110 cases. In the city of Bonn, icterus has been rarely met with, and not even the slight icteric hue of the sclera has been frequently seen by us; on the other hand Bäumler's observations are corroborated by Roth and Bergmann, who mention numerous cases of icteric hue of the conjunctivæ and of the skin, and also of distinct icterus catarrhalis. The official historian of the province of Merseburg asserts that all those cases which took a febrile course, no matter which form dominated the disease, presented a slight jaundice of the skin and the eyes, as well as slight pigmentation of the urine. We therefore see that this symptom seemed to be confined to certain districts, as it was in fact seen frequently, even constantly, in individual localities while it was not observed in others. At all events this slight form of icterus is not so characteristic that we can make use of it as a pathognomonic symptom in the diagnosis of influenza.

The spleen is found enlarged in many cases of influenza. But we find in a study of the literature the same striking difference in the reports as regards the occurrence of splenic lesions. Thus Birch-Hirschfeld and Jürgens have expressed themselves to the effect that, as a rule, no changes are to be found in the spleen, while Ribbert found the spleen in a few cases enlarged to more than double its size; in our cases at Bonn, and in eight autopsies he found a distinct increase in the volume of the spleen. Wallis and Leichtenstern also found some changes in a number of autopsies, and occasionally there was a considerable enlargement of the spleen. It is also mentioned by Drasche that an evident or even a quite considerable enlargement of the spleen was found in every case of influenza. Kuskow has studied the anatomical conditions of the spleen in influenza quite thoroughly. He found the organ enlarged, as a rule only slightly, twelve times in forty autopsies; in the other twenty-eight cases the spleen, curiously, is spoken of as having been small, and frequently markedly diminished in size. As characteristic lesions of a typical influenza spleen, he lays stress on the following: The capsule is wrinkled, the pulp is gray or of a dirty violet color, dotted with dark red points, and of the consistence of a rotten plum. Microscopically swelling of the endothelium in the veins and arteries is found, so that the lumen of the small arteries is not infrequently totally occluded. In other places we meet with thrombi of the veins and capillaries, along with extravasations of blood and tissue necrosis of the trabeculæ as well as of the pulp. The clinicians, on the other hand, in by far the greater number of cases, speak of the spleen as enlarged. Some of them characterize this splenic enlargement as being constant.

It was found in the City Hospital of Dresden in 80 per cent., in Hamburg in 56 per cent., by Bäumler in 63.5 per cent., by Schnaubert in St. Petersburg in 39 per cent. of the cases. On the other hand many observers have never been able to find enlargement of the spleen. In France the frequency of enlargement of the spleen is as a rule emphasized. In explanation of this extraordinary discrepancy Leichtenstern calls especial attention to the fact that the reason for it is probably not to be sought for in the greater or less malignancy of the influenza, nor in the complications with pneumonia or the especial involvement of the gastrointestinal canal; but that the different results arrived at are rather to be explained by the way in which the examination was conducted. This opinion of Leichtenstern is especially supported by the fact that a great part of the difference can be referred to the question whether the splenic enlargement is determined by palpation or percussion.

Of the other organs which belong to the digestive tract, the parotid gland is found occasionally diseased in influenza; this complication is, however, probably only rarely met with. Out of 55,263 patients in the German army, 12 presented this complication. Of 3,185 reports of the German collective investigation, 37 mention a complicating parotitis. In this as in previous epidemics a mixed infection was undoubtedly the cause.

In closing the description of grippal localizations in the abdomen, the inflammations of the peritoneum during the course of influenza should be mentioned. Leichtenstern writes that the grave form of grippal enteritis may lead to peritonitis, as a rule with fibrous, more rarely with purulent exudations, and mentions two of his own observations in illustration.

A boy, 12 years old, was suddenly seized with convulsions, high fever, and all the symptoms of a respiratory influenza. At the end of the second day terrible pains were felt in the abdomen, and there was retraction of the abdominal walls. The abdomen was extremely painful on palpation, particularly in the vicinity of the cæcum. Other symptoms were vomiting, constipation, and collapse. On the following day there was meteorism with diarrhœa, and death took place on the sixth day. At the autopsy there was noted a dirty, dark-brown discoloration of the peritoneum covering the lower portions of the small intestines and the cæcum. There were fibrinous deposits on the inflamed intestinal coils, but no liquid effusion was found in the peritoneal cavity. The mucous membrane of the lower part of the small intestine and of the cæcum and the ascending colon was of a dark-red color, the lesions being those of hemorrhagic enteritis. The appendix was intact.

A woman, 45 years old, presented the symptoms characteristic of a typical commencement of influenza (in the pandemic of 1889),

with a chill and high fever. On the third day symptoms of peritonitis (meteorism and vomiting) developed. At first two bloody passages occurred, followed by complete obstipation. On the eighth day, the fever still continuing, vomiting of fæces took place. In the left iliac region a large intestinal coil stood out like a tumor, and could readily be circumscribed. A surgeon called in consultation regarded this as v. Wahl's symptom, and declared the affection to be, in spite of the high fever, a volvulus of the sigmoid flexure. Operation was agreed on for the following morning. During the night the patient died. At the autopsy the intestines were found to be in a perfectly normal position; the peritoneum was of a dark-red color; a slight fibrinous peritonitis was present. The mucous membrane of the lower ileum was of a dark red color and swollen. The mucous membrane of the descending colon and of the sigmoid flexure, which was greatly distended and seemed thickened, was of a dark red color, in the condition of a "hemorrhagic membranous enteritis."

In the report of the German collective investigation, peritonitis is mentioned as having been present in two to three per cent. of the cases. Individual reports concerning its appearance may be found in the summary of the influenza epidemic in the German Empire by Paul Friedrich. Leichtenstern believes that there is no convincing evidence in literature that the influenza bacilli may reach the peritoneum primarily from the blood or from the intestine while the mucous membrane of the latter is intact, and cause its inflammation. I have seen a large collection of seropurulent fluid in the peritoneal cavity in one case, in a patient who was suffering from tuberculosis of the lung, and who died from the effects of an influenza pneumonia. The intestines in this case did not present any changes whatever, and there was no evidence that the purulent peritonitis had its origin from the intestines or their adnexa. The examination of the fluid found in the peritoneal cavity gave pure cultures of streptococci. A tuberculosis of the peritoneum could not be made out, so that I am constrained to believe that a secondary infection of the peritoneum by streptococci occurred as a metastatic inflammation, without the previous involvement of the intestine.

In another case I observed in an old man, probably 70 years of age, a grave form of peritonitis occurring several days after the beginning of the influenza, which led to death. The lungs were evidently affected in this case, for the patient suffered from a cyanosis of high degree, and rapid breathing. The temperature varied between 39° and 40° (102.2° and 104°), the pulse was irregular and weak throughout, the actions and speech denoted great nervous excitement. There was no reason to suspect a grave lesion of the intestines, for the bowels moved regularly although marked distention of the abdomen was present. In a few days the distention of the abdomen became excessive, the whole lower region of the abdomen

became tender on pressure, the liver was greatly enlarged, firm, and smooth, and the dependent portions of the abdomen contained fluid, which was found on exploratory puncture to be seropurulent in character. The man died, but an autopsy could not be obtained, so it must needs remain undetermined whether or not some inflammatory lesion of the intestine was at the bottom of this seemingly primary peritonitis.

Functional Nervous Symptoms.

In the symptoms of influenza those on the part of the nervous system are very prominent, and it may even be said that the picture of influenza is not complete in the absence of nervous phenomena. The frequency of nervous symptoms in influenza is also shown by statistics as to the participation of individual organs in the symptom complex of influenza. In the reports of the German collective investigation committee ninety-two per cent. of physicians dwelt especially on the nervous symptoms. On the other hand it has been accepted without protest that we are able to recognize a nervous form of influenza. In former epidemics the participation of the nervous system was recognized in the nomenclature of the affection, in that a neuro-rheumatic, neuro-cephalic, or neuro-synochal form of influenza was spoken of. The minute analysis of the nervous symptoms in influenza furnishes us with an extraordinarily large amount of interesting material. There is hardly a nervous symptom in existence which has not been observed in influenza, so that we should be compelled to discuss all the sensory and motor nervous symptoms of each part of the body, and should have to review with care the symptoms of disease of the central nervous system, including the psychoses, if we attempted to write an exhaustive treatise on the nervous symptoms occurring in influenza. We shall first take into consideration the general nervous symptoms, and then discuss briefly the most prominent of the individual ones.

Headache is a nearly constant subjective complaint of influenza patients; sometimes it is confined to the forehead, more frequently it involves the whole head. At one time it is described as a sensation of pressure, at another as a general hyperæsthetic condition of the scalp. In the latter case it frequently extends to the face, the ears, and the throat, and is combined at times even with a general hyperæsthesia of the whole body. In the greatest number of cases, the headache has its seat in the neighborhood of the forehead, over the eyes, extending from here into the depths of the orbits, and then frequently reaching such a degree as greatly to depress the patient or excite him to constant restlessness, or even drive him nearly frantic with the agony of it. The appearance of this headache may mislead us in

such a manner that it is taken for a meningeal symptom, especially as a true clouding of the sensorium is occasionally produced by the violence of the pain, its duration, and the insomnia which is caused by it, as occurs at times in grave organic disease of the brain. This violent cephalalgia not only attacks debilitated or susceptible individuals, but even strong men, who do not readily complain, lose control of themselves under the influence of these excruciating pains, and this probably for the reason that other nervous parts, besides the sensitive cerebral nerves, are at the same time affected by the influenza.

Backache.—No less a torture than the headache, although not quite so violent in their appearance, are the paroxysms of pain complained of in the back and the sacral region, radiating to the muscles, the joints, the thorax, and the extremities. While severe headache was complained of in about sixty per cent. of the cases, these pains in the back and sacral region were particularly mentioned in twenty-eight per cent. of those reported by the collective investigation committee. In many cases the patients complained of these in the beginning of the disease, and we may even count the sacral pains among the prodromal symptoms of influenza. They occasionally reach such a degree that the patient is unable to lie in bed quietly, every position becomes uncomfortable, and sleep is therefore disturbed and the patient's strength is exhausted.

Neuralgia.—In many cases the pain is localized in certain nerve areas, either at the beginning, during, or after the attack of influenza. There is not a nerve which has not been attacked by neuralgia in one or the other case. Trigeminal, occipital, cervicobrachial, and intercostal neuralgias have been observed with especial frequency, and have been particularly mentioned partly for their intensity, partly for the peculiarity of their temporary or periodic appearance. In these neuralgias the visceral forms are also to be included, violent pain in the stomach, in the course of the intestines, in the neighborhood of the bladder and of the diaphragm, and in the sternum. Thus Joffroy mentions more than six cases of severe neuralgia in the course of the nerves of the forearm and shoulder, in which, as shown by the accompanying symptoms of muscular atrophy, a neuritis must have been present. Leichtenstern has observed a very severe girdle pain which lasted for weeks, which was analogous to that occurring in tabes dorsalis, and was accompanied by paræsthesia of the lower extremities, ataxia being absent, however, and the reflexes being normal.

In the collective investigation reports, special neuralgias to the extent of 45 per cent. are mentioned by the recorders, a figure in excess of similar observations in previous epidemics. Nearly 14 per cent. of all recorders have described a trigeminal neuralgia in

individual cases. The neuralgias of the intercostal nerves are mentioned in these reports as 5.3 per cent., the neuralgias of the ischiatic nerve as 3.7 per cent. Each of these neuralgias has its own peculiar characteristic; a few appear periodically, so that they might be mistaken for malaria. A great many of the others are extraordinarily obstinate, so that they are prolonged far into convalescence, and may even last for years. I have often remarked that even after the disappearance of the neuralgias, painfulness on pressure over the affected nerves may remain for a long time, so that the patients themselves are frequently astonished at the tenderness of these spots, at a time when the pain has altogether ceased. Some observers place particular emphasis on the fact that the neuralgias of influenza usually become worse at night. In some cases of neuralgia, especially in intercostal neuralgia, herpes zoster has also been observed.

In connection with these neuralgias, *myalgia* should be mentioned as a prominent symptom. To these we may add the sacral pains, which have been mentioned above; there occur also violent pains in the extremities, sometimes accompanied by cramps. The muscles of the back, the thighs, and the calves are involved with especial frequency, and pressure on these groups of muscles increases the pain greatly. The pains then readily pass from the muscles to the joints. These muscle, limb, and joint pains were mentioned in the German collective investigations by twenty-seven per cent. of the reporters. These muscular pains may also be of very long duration, without the presence of any symptoms of atrophy to justify us in assuming that a true neuritis is present.

Among other nervous disturbances hyperæsthesia and anæsthesia of the cutaneous nerves are particularly mentioned, in part distributed over large surfaces of the body, frequently peculiarly localized. Leichtenstern described a case of total anæsthesia of the second division of the trigeminus. The hyperæsthesia may then also probably spread from the cutaneous nerves to the sensory nerves, and may thus give rise to remarkable morbid phenomena. We are especially reminded by the extensive hyperæsthesia of the skin, occasionally restricted to certain limbs, of meningitic or pseudomeningitic troubles. To these nervous disturbances are added paræsthesiæ, which are also developed in the skin and organs of sense, and which make themselves particularly felt in the nerves of smell and taste. Total loss of the sense of taste, total loss of the sense of smell, or of both together, has been observed in previous and recent epidemics; these symptoms also may outlast the attack of influenza.

Another symptom, which is mentioned by 12.6 per cent. of the reporters of the collective investigation, is *vertigo*, which is often

intense for only one or two days, but frequently lasts through the whole course of the disease.

Insomnia, which is of extraordinarily frequent occurrence, is also to be added to these nervous symptoms, and is one of the causes why the subjective sensation of weakness is so pronounced. Insomnia is frequently complicated by the appearance of delirium, often giving the impression when present as though the patient were sleeping and dreaming with open eyes, but which increases until pronounced attacks occur, reminding one in every way of delirium potatorum. In the collective investigations this delirium is mentioned by eight per cent. of the investigators as having been very irregularly spread over the various parts of Germany. This delirium is occasionally combined with mental disturbances, at times with an exaltation reaching the feeling of euphoria, at others with great depression. It is frequently observed that the patient suffers from limited attacks, in the intervals of which his mind is perfectly clear, and in which he is himself aware of having been delirious.

Attacks of *syncope* are also mentioned as an especially remarkable symptom. In the more recent epidemics, reports of the occurrence of syncope are more rarely met with than in previous ones. In the epidemic of 1510, those cases which were complicated with syncope were mentioned as belonging to a frequently occurring syncopal form of influenza, and the same form was observed in North America during the epidemic of 1874–75. Similar phenomena are the paroxysms of apprehension, which are, however, not so frequently met with.

A prominent nervous symptom is the exceeding *debility*, which is observed with extraordinary frequency, occurring in the form either of a sudden exhaustion and marked loss of strength, or of a long-continued feeling of debility. This prostratio virium is especially notable when no other severe symptoms of disease are present. Thus, it was observed in the last epidemic that in one of the greatest business houses of Berlin, employing one hundred and twenty men, more than one hundred of these were at one time, despite the greatest willingness, unable to continue their work, although not a single one was suffering from any serious disease. In the reports concerning the garrison at Munich, and in the records of the Prussian war department, cases are related in which healthy individuals who had only just entered the service presented the appearance within a very few hours of being exceedingly ill; they were hardly able to keep on their feet, and fell on their beds exhausted, where they usually lay on the side, unconcerned about what went on about them or what was offered them.

Postgrippal *neurasthenia* usually bears the character of the hypochondriac form, and is also met with in individuals who previously had seemingly no natural disposition to this temperament. In the treatment of these patients it is frequently very difficult to convince them that they are not suffering from any dangerous affection on account of their great bodily debility, and they cannot be convinced of their capability of greater exertion. The development of hysteria in persons who before their illness with influenza did not present any phenomena which could be looked upon as hysterical, has also been noted. Worms reports two such cases, one of hysterical convulsions in a girl ten years of age, and the other of sleeplessness, hallucinations, etc., in a nine-year-old boy, occurring on the eighth day of an attack of influenza and lasting a number of days. Hysterical forms of spasm and hysteroepileptic attacks, at times complicated with weeping spasms, are also mentioned by Grasset in the report of influenza in the German army. Hysterical jactitation in individual muscles (muscles of the abdomen) and hysterical tremor were observed, and also disturbances of speech and aphonia. In seven cases of severe postgrippal hysteria, which were observed in children by van Deventer, an hereditary or acquired neuropathic taint could always be traced.

As belonging to this general neurosis, we may also mention the so-called *comatose form* of influenza. Occasionally in the beginning or during the course of an influenza we may see a marked somnolence, increasing perhaps to coma, without any other cerebral symptoms. Friedrich Müller in Pforzheim observed a case of this form of coma which lasted fourteen days. In the spring of 1890, the newspapers were filled with reports that a new disease, called *noma* or *sleeping sickness*, had broken out in some parts of Italy. This disease presented symptoms which were similar to the observations of Krannhals, in which the clinical picture resembled that of a cerebrospinal meningitis which was not yet fully developed. According to the description of these cases of somnolence, appearing in an epidemic form, the greatest probability is that they were cases of influenza in which these comatose conditions were pronounced, as they may also be in hysteria. That they had accumulated in certain parts of the world, need not seem more remarkable to us than the fact, already frequently mentioned, that other forms of influenza have shown an inclination to make their appearance in a cumulative manner in certain localities at a certain time. Leichtenstern insists that this noma should be clearly distinguished from cerebrospinal meningitis, especially as pneumonia was a frequent complication. As regards the differential diagnosis between the coma of influenza and

that of diabetes, we may point to the fact that this condition in influenza is always accompanied by fever.

Motor Symptoms.—The nervous excitement occasionally finds expression in a chorea, which frequently makes its appearance only during convalescence. Among the motor symptoms, spasm of the muscles in the various areas are especially to be mentioned. Ripper reports a remarkable case: As a sequel of an attack of influenza a very severe pain appeared at the base of the thorax in a previously healthy man; at times it spread with increasing severity into the diaphragm, and radiated towards the nape of the neck and the shoulders. At the anterior insertions of the diaphragm, also on either side of the lateral portion of the neck and on the sternum, painful pressure points were found; soon a severe singultus made its appearance; this markedly increased when the patient talked, and was accompanied now and then by yawning and vomiting; the hiccoughs occurred one hundred times in the minute. After from ten to twelve days all symptoms disappeared. Grave motor symptoms were observed in a woman, forty-nine years of age, by Leichtenstern. Following influenza she had girdle pains of the trunk and violent pains in both lower extremities, accompanied by increased patellar reflexes and foot clonus, with disturbances of sensation, marked ataxia, and great weakness in the extremities. There was also incontinence of urine with cystitis. The woman made a perfect recovery. In another patient Leichtenstern observed during a typical attack of influenza a very peculiar clonicotonic spasm of the muscles of the whole body, so that they were at times thrown into a tetanic condition. This alternated with tetanoid tonic spasms of the fingers, accompanied by a peculiarly bizarre spasmodic position of the fingers or of the forearms and of the lower extremities, also by stiffness of the neck, without meningeal symptoms. Unilateral spastic convulsions of the face have also been noted.

A case has been reported in which these spasms appeared in the right half of the face and in the extremities of the right side. Symptoms of paralysis occurring in peculiar distribution over the lateral half of the body, and similar to these spasms, which very strongly remind one of hysterical conditions, have also been observed. In all the nervous phenomena thus far described, we are obliged to seek an explanation in the action of some soluble toxin. No matter how violent the symptoms may have been in individual cases, no matter how peculiar was their localization, or of how long a duration they were in some cases, they had this in common that they were all purely functional disturbances. The proof of this is found in the fact that the combination of nerve symptoms with atrophy was not sufficiently

marked to justify a diagnosis of anatomical changes in the nerves themselves. On the other hand recovery has frequently resulted in such cases with astonishing rapidity; severe neuralgias have suddenly ceased; total paralysis, which seemed to justify the diagnosis of a severe lesion of the peripheral or central nervous system, frequently has disappeared with marvellous rapidity. This could not have occurred if anatomical lesions in the centres or the nerves had been present. We must not fail to mention furthermore that the action of a drug, for example, antipyrin, salipyrin, or quinine, frequently caused a change for the better or even a perfect cure so suddenly that the diagnosis of a functional nervous disturbance was forced upon us *ex juvantibus*.

Neuritis.

In opposition to the previously described cases, observations have accumulated which show that material lesions may arise in individual nerves or in many nerves at once. Here the morbid picture is changed by the addition of symptoms of multiple neuritis, which also appear as sequelæ of other infectious diseases. Such a disease of the nerves is known to us especially as a consequence of diphtheria. It may, however, also occur after pneumonia and after typhoid fever; in rare cases also after measles and scarlet fever. We are familiar with the fact that the toxins are capable in these various acute infectious diseases of producing inflammatory changes in the nerves, but it is nevertheless astonishing how extensively these nerve inflammations occur in influenza. I will not even maintain that all those cases which have been described in the preceding section were only of a functional nature, for there may have been many true neural affections among them. It is in truth very hard to draw a sharp dividing line between the functional and the organic neural diseases. It is probable, however, that many more cases are diagnosed neuritis which are really functional only, than the reverse.

Helfer has reported a case of abasia-astasia following influenza. A girl, ten years of age, became ill of grippe in January, and could not maintain the upright position when it came time for her to leave the bed, so that she was obliged to keep her bed continuously up to May. The mother carried the child on her back, the child clinging with her arms about the mother's neck, and grasping the hips of the mother with her legs. When the child was examined in the recumbent position, no sign of disease could be demonstrated, except a tenderness of the upper dorsal vertebræ. Motility, sensibility, and reflexes were all normal. But when the child was placed on her feet, the knees gave way under her. After a period of eight days she was again able to stand when sup-

ported; after fourteen days she could walk around, holding on to the furniture. After three weeks she could walk with a cane, and after four weeks she had fully recovered. There are, however, very many capable observers who have reported cases of true neural disease, with symptoms in the sensory, motor, and coordinating spheres. Often the seat of this form of neuritis is found only in a certain branch of the nerve, being shown by pain, paræsthesiæ, and paralysis, but more frequently the distribution is much greater, and we have the picture of a polyneuritis of influenza. This polyneuritis may make its appearance with such violence and spread to such an extent, that the picture of an acute ascending Landry's paralysis may be perfectly simulated. Cases like these have been described by Kahler and Eisenlohr. Macphall has reported four cases of peripheral neuritis which occurred in conjunction with attacks of influenza. The first case involved the upper and lower extremities, the second only the lower; both recovered. The third case ended in death from atrophy of the lower extremities, disturbances of the bladder, psychic disorders, and paralysis of the diaphragm. In the fourth case there was present a paresis of the peroneal muscles accompanied by sensory disturbances and loss of the patellar reflexes. Recovery in this case was complete. Another interesting case has been described by Monro.

A woman, 31 years of age, complained of pain in the upper extremities after recovering from an attack of measles, which continued for a few months, and made its appearance again after an attack of influenza. Neuritic pains were present in both arms, debility, tenderness on pressure over the nerve branches, paræsthesia, and diminished tactile sensibility in the hands. Recovery followed in two months.

Joffroy has described cases of neuritic paralysis in which besides the motor paths the sensory were also involved in a violent neuralgia. A case of Bosser should also be mentioned here, in which a paralysis of all four extremities existed. Two interesting cases of neuritis multiplex following influenza have been reported by Westphal.

In the first case a man, 29 years of age, was seized with a general chilliness seven days after the beginning of influenza, and a sensation of formication and numbness in the finger-tips, afterwards also in the toes, and to this was added, at the end of a week, weakness of the legs and arms, and difficulty in swallowing. With all this there was no fever. Syphilis and alcoholism were excluded. Examination revealed a lessened motor power of the arms and legs, the faradic irritability of the nerves and muscles being retained, and the muscular tissue being strongly developed; insecure, staggering gait, loss of the patellar reflex and those of the biceps and triceps tendons, the abdominal and cremaster reflexes being retained. There was a seemingly

slight facial paralysis of the right side. In a few weeks all these symptoms improved under treatment by zinc baths, douches, and faradization, the patellar reflexes only were still absent at the end of four weeks. There were no marked sensory disturbances, the bladder and rectum were normal, and there were no pupillary symptoms.

The second case was that of a merchant, 25 years old, who was affected about a week after an attack of influenza, during an eruption of urticaria, by a motor paralysis, which, commencing in the lower extremities, gradually extended in the course of two weeks over the whole body; some cerebral nerves were also involved, as shown by a left lateral facial paralysis, which also spread to the right side, and by difficulty in deglutition. At the same time the reflexes died out and muscular atrophies and nutritional disturbances made their appearance. During the increase of the paralytic symptoms the various nerve trunks were tender on pressure and the muscles were very painful on slight handling.

Except for paræsthesiæ of a slight degree no sensory disturbances were at any time noticed. After the disease had remained stationary for two weeks, rapid improvement occurred and advanced to nearly perfect recovery. Vasomotor and trophic disturbances at the same time appeared, as manifested by œdema of the lower extremities and a strong growth of hair on both lower and upper extremities.

While, as above remarked, the differentiation of neuritis from functional disturbances presents some difficulty when the inflammation is limited to single trunks, polyneuritis is also with great difficulty clearly distinguished from central nervous affections. It may be seen from the previously described cases that whole groups of muscles frequently become paralyzed simultaneously, so that we are compelled to agree with Leichtenstern when he asserts that many of these cases have in all probability as their foundation circumscribed lesions, caused by the toxins of influenza in the motor nuclei of the middle and fourth ventricles, and should therefore be looked upon as nuclear pareses. He would especially include here certain combined forms of paralysis of the muscles of the eye, of the soft palate, and of the œsophagus—groups of muscles which, combined for the purpose of acting together, are supplied by common nuclear centres. He emphasizes the fact that the material for experimentation is exclusively a clinical one, mainly by reason of the favorable course usually taken by these forms of paralysis. We are therefore not yet in the possession of observations which will enable us to decide whether neuritis or disease of the nuclei, or functional toxin poisoning, or inflammatory degenerative processes in the nerves and in the nuclei themselves are anatomically at the bottom of the disease. Only one thing he considers as common in all these cases, namely, that gross anatomical changes cannot possibly be present, because of the absence of all grave

cerebral, bulbar, or spinal symptoms. Leichtenstern has grouped all these cases as follows: Isolated paralysis of the soft palate, paralysis of accommodation without paralysis of the soft palate or of the muscles of the œsophagus; intermittent paralysis of the accommodation, paresis of the rectus internus, insufficiency of the internal recti; paralysis of the rectus superior, of both superior oblique muscles, of the oculomotor, of the abducens, either uni- or bilateral; hemilateral mydriasis, nuclear paralysis of the eye muscles; polioencephalitis superior; semilateral paralysis of the hypoglossus, accompanied or not by atrophy of the tongue; paralysis of one recurrent nerve, bulbar nuclear paralysis, isolated paralysis of one facial nerve; total paralysis of one arm, atrophic paralysis in the area of individual nerves of the chest, shoulder, or upper arm, of the deltoid, supra- and infraspinatus, trapezius, and serratus magnus—"type scapulohuméral."

All these affections are met with in influenza, in the most diverse manner, or rather much more mixed than we are usually accustomed to meet them among the neuritic sequelæ of other acute infectious diseases. Most of them do not make their appearance immediately with the attack of influenza, but occur later, and are as a rule entitled to a much more favorable prognosis than neuritis which is to be referred to other cases.

Encephalitis.

Extraordinarly grave diseases, which frequently end in death, are caused by influenza under the picture of severe forms of cerebral paralysis. These may appear as mono- and hemiplegias, or may be complicated with grave cerebral symptoms, coma, insensibility, convulsions, and delirium. Our attention was first drawn in the spring of 1890 to these grave apoplectiform affections by Leichtenstern, who reported at the time no less than eight of these cases, and was able later to add four more. Up to then no allusion to this important complication had been made in literature. These cases all had in common the occurrence of a hemiplegia or monoplegia at the height of or immediately following a typical case of influenza, also the fact that the hemiplegia was always accompanied by more or less pronounced, usually very high fever, and that the fever again rose on the occurrence of the hemiplegia, while violent headache or other symptoms which might be taken for signs of meningitis were generally absent. In view of the importance of this grave form of the disease, it will be profitable to cite briefly these observations of Leichtenstern.

A well-nourished woman, 56 years of age, was taken on December

20th with the typical symptoms of a mild influenza; she complained of moderate headache and coryza. Temperature, 38.1° to 39.3° (100.6° to 102.7°). On the morning of December 22d, the temperature rose to 40° (104°) accompanied by marked apathy. The nervous symptoms increased during the afternoon to somnolence and paralysis of the left facial and hypoglossus nerves, and of the left arm. The lower extremities were freely movable; there was stiffness of the neck. On the following day there was coma, accompanied by high fever (40.3° = 104.5°), and towards evening death occurred. An autopsy could not be obtained.

A very strong, healthy man, 42 years of age, was taken with sudden coma, a fever of 40.5° (105°) and a total right lateral hemiplegia on the fourth day of a typical, slight influenza; there had been no previous complaint of severe headache or stiffness of the neck. Death occurred two days later, the fever remaining high. No autopsy was had.

A man, 36 years of age, suffered from a typical case of influenza. On the sixth day, when the fever had already disappeared, the patient complained of a "weakness" of the right arm, in the afternoon also of a similar weakness of the right leg. He had no headache and no aphasia. In the evening he had a total paralysis of the right arm and marked paresis of the right leg, but there was no sign of a paralysis of the facial and hypoglossus. There was no fever. The paralysis slowly disappeared and finally recovery ensued.

A woman, 48 years old, had a typical influenza, on the fifth day of which a severe bilateral pneumonia made its appearance. On the twelfth day from the beginning of the influenza, when the fever had already disappeared, the patient on awaking in the morning was markedly somnolent. The physician who was called found a complete left lateral hemiplegia. At the same time a continuous high fever had again appeared. Stupor now developed. There was œdema of the paralyzed lower extremities. The patient was still under observation at the time the report was made; the paralysis had persisted and there was only a very slight improvement in the stupor.

Patient, 56 years old, who had always been a healthy man, was taken ill with influenza on December 25th. On December 29th, he suddenly experienced severe symptoms of vertigo and a total aphasia, retaining his mental power however. He had paresis of the right facial and hypoglossus, and weakness of the right upper extremity. On dismissal, January 8th, 1890, the patient was in a perfectly normal condition.

A man, 32 years old, had a typical attack of influenza, the fever leaving on the second day. On the fourth day the patient, while sitting at his meal, was suddenly seized with a violent headache; at the same time chilly sensations were experienced and the temperature rose, reaching towards evening 40.2 ° (104.4°). He passed a restless night, without delirium however. On the following morning the headache was better, but now a paresis of the right upper extremity came on, without the slightest symptom of a facial paralysis. There

was no aphasia present. On the afternoon of the fifth day a nearly total paralysis of the right arm occurred. The fever now abated, and on the sixth day the temperature was normal. On the ninth day a nearly complete return of the normal power of movements in the right arm had taken place. A perfect recovery rapidly followed.

Patient, 27 years old, had a typical, mild influenza, accompanied by slight headache. On the fourth day, after the temperature had become perfectly normal, a violent chill, followed by vertigo and vomiting, suddenly occurred. In the evening the patient was found to have considerable paresis of the right facial, a slight one of the hypoglossus, and a paresis of the right upper extremity. Somnolence and aphasia were noted. On the following day the temperature became normal. The symptoms of paralysis gradually disappeared within eight days. Perfect recovery followed.

In the following case in which an autopsy was permitted, an explanation was found of the symptoms observed during life, and in all probability one or all of the cases just described were to be explained in the same way.

A healthy woman, 25 years of age, was suddenly taken ill at breakfast with a chill, which lasted for some time, so that she was obliged to take to her bed at once. She complained but little of headache, but she was remarkably irritable. She had frequent vomiting. Towards evening the temperature rose to 39° (102.2°) and apathy was noticed. At ten o'clock in the evening there was absolute unconsciousness and the temperature was 40.3° (104.5°). This coma with an elevated temperature (as high as 40.7° = 105.2°) continued to the fourth day of the disease (three o'clock in the morning) when death occurred. The urine was normal. No other symptoms except the grave cerebral symptoms were present. On the first and second day a moderate stiffness of the neck could be demonstrated. A diagnosis was made of foudroyant influenzal meningitis. The autopsy disclosed an interesting condition. There was slight pachymeningitis hæmorrhagica interna on both sides. The pia at the base of the brain was absolutely normal. The cerebral arteries were also normal, and no emboli were to be discovered anywhere. The pia covering the convolutions was intensely cloudy and injected, here and there presenting points of hemorrhage or diffuse infiltrations of blood the size of a dollar. Along the larger vessels of the pia covering the convexity were streaks of an evidently purulent exudation. The pia could not be peeled off without bringing with it portions of red softened cortex. In the cortex were found scattered through all the convolutions large and small, intensely congested, stippled, that is, hemorrhagic, softened areas, of a diffuse grayish-red color. Thus the lesions were those of hemorrhagic encephalitis occurring in foci, and hemorrhages of the pia also in foci. The rest of the brain did not present particular changes, especially no inflammatory or hemorrhagic foci in the interior of the brain, or in the ganglia, the pons, the cerebellum, etc.

Leichtenstern observed such generally multiple, hemorrhagic,

encephalitic foci a few times in 1885–86, at autopsies in cases of epidemic cerebrospinal meningitis, in which these foci were found to be the cause of the hemiplegias occurring in the course of an epidemic meningitis. Exactly the same picture of numerous, enclosed, hemorrhagic or softened foci in the cortex of the brain is occasionally met with in endocarditis ulcerosa, where they undoubtedly are caused by capillary emboli.

Recently Leichtenstern has described four other cases of acute focal hemorrhagic encephalitis, which he does not class positively among cases of acute influenza, on account of the absence of marked symptoms of influenza. They belong to the cases which Strümpell has since described under the title of "primary acute encephalitis," and are undoubtedly to be referred to microbic embolism. Fürbringer has reported two cases of grave organic cerebral affections following influenza, in which large hemorrhagic foci were found after death, which perfectly resemble those observed by Leichtenstern as well as others seen by Senator and Virchow.

A domestic, 27 years of age, of strong build and well nourished, suddenly noticed in the middle of the night that sensation had become indistinct in the right arm, and that the arm was weak. This symptom disappeared during the following days, but the patient complained of exhaustion and anorexia, with increasing debility. After about two weeks, during which the patient had somewhat recuperated, headache, nausea, and great lassitude suddenly occurred; on the following day loss of sensation again returned in the right arm and was accompanied now by right hemiplegia, somnolence, vomiting, and general convulsions, which lasted one hour and recurred from time to time. The woman was unconscious; she could not be aroused by calling, but when pricked with a needle she responded by painful distortion of the face. The latter was cyanotic; the eyes were closed, and on separating the lids horizontal nystagmus was noticed. The pupils were of medium size, but did not react to light. There was grinding of the teeth, with occasionally long-drawn yawning. There was continuous jactitation, with an inclination to right lateral decubitus. The extremities were at times perfectly flaccid, at times somewhat rigid. The patellar reflexes were increased and there was incontinence of urine. Temperature, 37.4° (99.3°), pulse 84, hardly abnormal. One hour later there was jactitation of the facial muscles and of the extremities on both sides. The pulse was fuller and slower (48), and there was snoring respiration. The patient reminded one of a person under the influence of chloroform. On the following morning the convulsions were repeated. The temperature, which had fallen to 36° (97°), rapidly rose to 39° (102.2°). Examination of the fundus of the eye, during which there was a clonus in the area of the right facial, and later of the whole body, revealed strong injection of the veins of the choroid. Spasmus nictitans and jerking of the alæ of the nostrils were especially marked. The face was now red-

dened. The temperature rose at noon to 40.1° (104.2°), later to 40.8° (105.4°); the pulse was small and between 88 and 100; the respirations were 36 to the minute and regular. There was flaccid paralysis of the extremities, and the patellar reflexes were now absent. Death took place in the evening, the patient having never regained consciousness.

The autopsy showed an intact valvular apparatus of the heart, a severe purulent bronchitis, and small disseminated bronchopneumonic foci. The spleen was enlarged, congested, and soft. In the neighborhood of the omentum there were some large punctate hemorrhages. The mucous membrane of the small intestine was swollen in its middle portion for a distance of about six feet, and dotted with numerous points of hemorrhage and in places infiltrated with diffuse hemorrhages. The longitudinal sinus equally with its tributary veins was filled with a dark red, adherent, rather tough coagulum, as were also most of the larger pial veins of the convexity. The pia was intensely hyperæmic, readily peeled off from the surface of the brain. In each cerebral hemisphere near the central convolution was a hemorrhagic focus the size of a hen's egg, with liquid contents consisting of blood and disintegrated cerebral matter. Both apoplectic foci, which embraced both the gray and white substance, were surrounded by a zone, some centimetres broad, reaching deeply into the brain substance, slightly yellowish tinted, softened and dotted with innumerable punctate hemorrhages. A somewhat smaller similar focus, the size of a walnut, containing less blood, was situated on the edge of the right occipital lobe.

A merchant, 32 years old, of previous good health and fairly well nourished, was suddenly taken ill on November 13th with headache, severe pain in the sacrum, much cough, moderate fever, acute indigestion, and a feeling of exhaustion. In spite of being ordered to bed he pursued his occupation, and on November 18th felt so well again that he ate some caviar and meat and drank some beer in the evening. On the following morning he complained of great nausea, vomiting, and a feeling of weight in the stomach. The family physician again found slight fever, retracted abdomen, and great restlessness. The latter increased on the following day, and the sensorium was dulled. On the 21st, the pupils were contracted and reacted slowly to light, and stiffness of the neck was present. In the afternoon the patient was found unconscious, throwing himself about wildly in bed. The breathing was rapid and nasal. There was incoordination in the movements of the eyeballs. The urine was passed involuntarily. Diffuse bronchial râles were heard over the lungs. The patient was taken to the hospital with a diagnosis of "meningitis," and arrived there in a comatose condition. The eyeballs diverged in the most diverse directions, the pupils only slowly responded to light. The fundus of the eye did not present anything unusual. The patellar reflexes were somewhat exaggerated; the pulse was 76, respiration 16, temperature on admission was 36° (97°), a few hours later 38.9° (102°). There was extreme restlessness. The following day the temperature was 40° (104°), the pulse small and frequent. In the evening the temperature rose to 40.6° (105°), respiration 56; œdema of the lungs came on and the patient died.

At the autopsy was found a hemorrhagic encephalitis of very unusual extent and intensity. Nearly the whole of the great central ganglia of both sides was softer than normal, partly a diffused red, partly yellowish in spots, and dotted with numerous punctiform and linear hemorrhages, especially in the region of the white matter. Similar smaller foci were found in the crura cerebri, cerebellar hemispheres, and pons. The heart was normal. In the lower lobes of both lungs there were larger and smaller foci of bronchitis.

Other cases of a similar nature have been described by Kohts as forms of paralysis and pseudoparalysis occurring in childhood after influenza. In four cases the author found gross lesions of the brain as the cause of the paralysis. Similar focal diseases of the brain have been reported by Bristow, who observed five cases in which the preceding influenza was looked upon as the etiological factor in the encephalitic process. The autopsy revealed large abscesses in the cerebral tissue. Koenigsdorf has also described a case of acute hemorrhagic encephalitis. Leichtenstern says that in these cases we are dealing with sharply circumscribed foci of different sizes, from the size of a cherry pit to that of a pigeon's egg. By the confluence of neighboring foci, still larger extensions are formed. Sometimes only one such focus is present, frequently a number of foci justify the name of multiple encephalitis. Its nearly constant seat is the gray matter, most frequently it is found in the cortex of the cerebrum and in the central ganglia, much less frequently in the crura cerebri, pons, and cerebellum. From the cortex of the brain or the central ganglia, the encephalitis occasionally spreads in a wedge-shaped form into the white substance of the hemispheres. In this case we meet with a notable symmetrical localization of the foci in both cerebral hemispheres. The encephalitic focus consists, in its typical form, of innumerable, closely crowded, very fine, hemorrhagic points, resembling flea-bites, between which the tissue, more or less softened, is of a gray to a reddish-gray color. Through secondary hemorrhages into the softened centre, larger hemorrhagic foci may form. It cannot be doubted that such cerebral hemorrhages in influenza have been looked upon frequently as primary apoplexies, when in fact they were due to secondary hemorrhages into encephalitic foci, which had softened in the centre. The veins occasionally become thrombosed. This thrombosis may spread still further into the superior cerebral vein and the longitudinal sinus, or from the veins of the corpus striatum and optic thalamus into the choroidal veins, the internal cerebral vein, the straight and transverse sinuses. In this case the diagnosis between primary encephalitis and primary thrombosis followed by secondary foci of hemorrhagic softening is possible only by the use of the microscope. Grippal encephalitis is occasionally complicated by hemor-

rhagic meningitis involving both pia and dura. Lines of purulent exudation running parallel with the vessels of the pia are only exceptionally met with. The classical description of Leichtenstern will be of extreme value for our guidance in such cases.

As to the symptoms of this form of encephalitis, it goes without saying that they will depend greatly on the situation and the extent of the foci. Since the large encephalitic hemorrhages and areas of softening are composed of a great number of smaller foci, we may readily understand how these small foci will be found variously disseminated through the cerebral tissue. This explains the manifold symptoms of paralysis in individual nerve areas. In the differential diagnosis of this form of paralysis from the neuritic affections we must bear in mind that the encephalitic occur at the height of the disease, that they are accompanied by fever, while the neuritic affections, as above remarked, make their appearance in the majority of cases subsequent to an attack of influenza. Leichtenstern reports that no positive case is known in which an acute grippal encephalitis, by localization at the floor of the third or fourth ventricle, has led to an acute hemorrhagic polioencephalitis superior or inferior.

If the seat of the encephalitic foci does not affect the motor centres and paths, all motor symptoms of irritation and paralysis may be absent; for this form Leichtenstern also reports a case in which unconsciousness and coma suddenly occurred during high fever, and were followed by death. The autopsy disclosed the seat of the encephalitic foci to have been the apices of both frontal lobes and the right temporal lobe. Of course, not every case of cerebral hemi- and monoplegia should be looked upon as the result of hemorrhagic encephalitis. In these cases thrombosis and embolism as well as local hemorrhages play a practical rôle even without softening. Abscesses of the brain may, on the other hand, also occur independent of hemorrhagic encephalitis. Just as cerebral abscess may occur in purulent bronchitis, so there is a possibility in influenza that abscesses may be formed in various parts of the brain by the dissemination of bacteria. Furthermore, just as we have seen in the case of symptoms pointing to an affection of the peripheral nerves, we may have grave cerebral symptoms caused by the local action of the toxins of influenza without the presence of the grave lesions of an encephalitis or of an abscess.

As regards the course of this disease, we are not able to lay down a general rule applicable to all cases. In the fatal cases examined post mortem there was found extreme encephalitic disintegration. If, however, we take into consideration the gravity of the clinical symptoms observed in certain cases in which recovery ensued, we cannot

doubt that just as extensive changes of the brain have in other cases gone on to recovery. It is also possible for abscesses to exist in the brain for a long time without any symptoms, and then for some reason suddenly to find expression in very dangerous symptoms. That smaller hemorrhages may heal without leaving any symptoms behind is as true of influenza as it is of capillary apoplexies due to other causes.

Pfuhl in 1892 endeavored to prove that the influenza bacillus exists in parts other than the respiratory system much more frequently than was at first supposed, and that it is to be found with especial frequency in the central nervous system in fatal cases of influenza. It was urged against Pfuhl's earlier observations that it was not the influenza bacillus that he found, but in a later publication in 1897 he has described three cases in corroboration of his earlier ones in which he claims that he has really proved the existence of the influenza bacilli in the brain. In his first case the disease lasted from the beginning of December, 1895, to March, 1896. The patient had during this time experienced a very marked improvement, so that he was able to leave his bed. Especially important was it that, in conjunction with salivation and abnormal sensations of taste, and also extreme trophic disturbances, such as the formation of boils and blisters on the integument of the neck, there was present a continuous cardiac debility which led to extensive thrombi. Of the nervous symptoms in this case were especially important the violent sudden headache, pains in the limbs, and great tenderness to pressure at the points of exit of the nerves, especially at the upper border of the orbital cavity, and following this stupor and slight stiffness of the muscles of the neck. There were grave symptoms on the part of the lungs, and later on pain and stiffness of the right arm; vomiting occurred a number of times, and there was numbness of the mouth. The trophic disturbances were accompanied by bedsores in the sacral region and on the heels, also by œdema of the left leg. Death took place from cardiac paralysis.

The second case was marked from the beginning by severe headache and vertigo. Pulmonary symptoms were slight, but diarrhœa occurred. Great restlessness and later delirium and involuntary evacuations were noted.

The third case, which ended in death within three days, was remarkable on account of the sudden occurrence of deep stupor and the presence of choleraic symptoms. This case was interesting from the fact that the patient, shortly before taking sick, had been bitten in the right arm by a horse, so that one might readily have suspected an infection from this source. In the diseased portions of the brain

there was a pronounced infiltration of the ganglia of the cerebral cortex. A notable destruction of the ganglion cells bore witness to the active advance of influenza bacilli. The results of bacteriological investigation, and especially the rapid ending of the cases by death, led Pfuhl to the conclusion that the central organs of the nervous system were involved fatally only in those cases in which the excitors of the disease had lodged there and had become virulent. We may now take it as proven that influenza bacilli are capable of exciting suppuration. The primary purulent bronchitis in influenza and the formation of abscesses in the lungs, when the common pus cocci are absent, have taught this to us. As, however, the influenza bacilli are able to invade the tissues as a whole, it is easy to imagine that they can excite metastatic abscesses. This does not, it is true, seem to occur very often. Primary, purulent, encephalitic changes may be induced by metastasis to the brain, but another cause of the formation of purulent encephalitic foci is to be found in purulent inflammation of the ear, the frontal sinus, the antrum, or the nose. Purulent otitis, a frequent affection in influenza, may extend by continuity from the bone to the meninges and into the brain tissue. It is possible also that secondary purulent foci may be developed from a purulent tonsillitis.

Meningitis.

In the same manner in which various mixed infections accompanied by pus-forming cocci make their appearance in influenza, purulent inflammations also occur in the meninges, which are to be ascribed to this addition of other bacteria. It is not always possible to trace the route which has been travelled by these bacteria. When they reach the meninges from the ears or the nasal cavities, the close contiguity of these parts makes the explanation easy, provided we assume that bacteria can pass by way of the lymph channels. Diseases in distant parts may also be the cause of a purulent meningitis, as we see in the case of pneumonia, when the common pus cocci and with them also pneumococci are found in the purulent meningeal exudate. The presence of influenza bacilli in the pus of the meninges is affirmed by Pfuhl. Clinical observation has demonstrated the possibility of a primary purulent grippal meningitis.

Leichtenstern in 1890 described four cases of this kind which ran a very acute course, ending fatally, in which the true nature of the disease was shown by the results of the autopsy. In two cases occurring at the City Hospital at Cologne, a purulent meningitis of exclusively basilar location was found in one case, and in the other the same condition involving the convexity. Both cases presented at the same

time a purulent spinal meningitis of the same appearance as we are wont to observe it in epidemic cerebrospinal meningitis. In none of the cases examined post mortem was there present the connecting link, so to say, of an empyema of the frontal or ethmoidal sinus, and the acute course also made it probable that the agent of infection was carried directly by the lymph paths from the nasal cavity to the subarachnoid spaces. The following case was reported by Fürbringer:

The wife of a laborer, aged 50 years, was admitted on November 29th, 1891, in a moribund condition. The woman had been taken ill two weeks previously with fever, cough, and pains in the head, throat, and abdomen, accompanied by anorexia, diarrhœa, and marked weakness of the limbs. A few days later pain appeared in the left thigh, then came swelling of the left arm. During the last few days insomnia, restlessness, stupor, fear of the bed, loud screaming, and hallucinations were added.

On admission the patient had a medium degree of fever, no pulse was perceptible, there was an alarmed expression, the pupils did not react to light, the lips were parched, and the tongue was coated. The lower extremities were flexed on the abdomen and rigid. When attempts were made to straighten them, the patient complained loudly of pain. The stools were diarrhœal and were passed, together with the albuminous urine, in the bed. The abdomen was soft. Occasionally the patient would scream out. Both arms were greatly swollen, of a pale red color, in part cyanotic. There were copious râles over the lower portion of both lungs. Death occurred within six hours. At the autopsy the arms were œdematous, the epidermis in some parts hanging in tags, the corium was reddish-brown, and the muscles beneath were dark red, studded with hemorrhagic infarctions, and easily torn. There was not a particle of pus present. Neither emboli nor thrombi were found in the vessels. There was leptomeningitis of the convexity on the left side behind the central convolution, where there was an area the size of the palm of the hand infiltrated with pus. Broad trails of pus ran parallel with the blood-vessels. There was no purulent otitis. The brain itself did not present any lesions. There was a purulent bronchitis. The spleen was enlarged, hyperæmic, nearly pultaceous. The kidneys were dotted with small hemorrhages.

These purulent forms of meningitis are, on the whole, among the most frequent complications of influenza. This has been corroborated by the observations of Arzél, Huysmann, and Maillard. Revilliod has also published a case of this kind.

A woman, 60 years of age, had passed through a pneumonia, and had reached a perfectly afebrile period of convalescence, when she suddenly became comatose and died on the twenty-first day of her illness. The autopsy disclosed an extensive purulent meningitis, and a purulent effusion into the ventricles.

The appearance of meningitic symptoms in influenza must be

studied from different points of view. We must remember that grave meningitic symptoms may be due to a curable condition or may even be the evanescent effects of some poison in the brain. On the other hand, encephalitic affections of the brain are sometimes accompanied by symptoms which lead to the diagnosis of an involvement of the meninges. A third group is represented by meningitic affections, which are not a part of the influenza itself, but belong to pneumonia occurring secondarily to the influenza. Meningitis, we know, is frequently met with in croupous pneumonia, but we must not forget that in some cases in which a pneumonia complicates a meningitis, the former may really be a sequel of epidemic cerebrospinal meningitis. The differential diagnosis between a grippal meningitis and the various complications spoken of will therefore under certain circumstances be extremely difficult, especially so when the influenzal meningitis runs a very acute course. The course of the disease may be so rapid indeed that a perceptible purulent exudation has not yet occurred in the meninges. According to Leichtenstern, we find most frequently in influenza a meningitis of the convexity marked by an intense cephalalgia, early stupor, and an absence of stiffness of the neck. If the meningitis has its seat at the base of the brain, its differentiation from epidemic cerebrospinal meningitis is a matter of the greatest difficulty, and frequently is impossible. Both are ushered in suddenly with high fever, and stiffness of the neck is one of the earliest symptoms. We may, however, by lumbar puncture obtain some of the cerebrospinal fluid, which may be bacteriologically examined, and the presence of the meningococcus in such a case will determine the diagnosis. Leichtenstern has never met with secondary pneumonias in meningitis, so that a combination of pneumonia and meningitis either justifies the assumption of an inflammatory affection caused by the diplococcus, or, if symptoms of influenza also occur, we may assume it to be an influenzal meningitis. In distinguishing a grippal meningitis from one due to tuberculosis, it is said that the tuberculous meningitis does not begin suddenly, as is the rule in the grippal form, with a chill and high fever. I am, however, not able to subscribe to this statement. I have seen tuberculous meningitis run a very rapid course, and I especially recollect the case of a child in which brain symptoms of extraordinary intensity suddenly made their appearance when the patient awoke in the morning after a quiet night. Death followed on the evening of the same day, with high fever, over 41° (106°), after rapidly occurring coma. At the autopsy a miliary tuberculosis of the meninges was found.

Krannhals observed meningeal complications in a typical case of

fibrinous pneumonia, and in one case of catarrhal pneumonia; he also saw five cases of purulent meningitis, of a tuberculous or traumatic nature, occurring during the influenza period. At the autopsy a meningitis was demonstrated, but no otitis, nor any suppuration of the petrous portion or of the frontal sinuses. In single cases the meningitis was diffuse; in others, large purulent deposits were found in the chiasm and the pons. In one case an abscess, of the size of a bean, filled with pus, was found in the left gyrus supramarginalis, near the surface, which had perforated into the arachnoid connective tissue. In a number of cases he demonstrated streptococci and diplococci in the exudation from the meninges. Krannhals also says that influenza may lead to a hemorrhagic leptomeningitis without either serous or purulent exudation in the meninges. According to Leichtenstern this is analogous to the metastasis of the germs to the pia mater, producing hemorrhagic encephalitis, such as has been described by him. Hemorrhage plays an important rôle in these processes, but it remains doubtful in what manner suppuration is connected with these hemorrhagic conditions.

Kuskow has described under the title of hemorrhagic grippe cases of simple hemorrhage of the cerebral meninges, especially of infiltrations of blood into the pia, without a trace of inflammatory infiltration. Erlenmeyer refers a peculiar case, observed by him, which ran its course, with the symptoms of Jacksonian epilepsy, to a hemorrhage.

Cases which correspond to those previously described have been named pseudomeningitis grippalis, especially by French investigators. The cases simulated meningitis in every particular, but they either ended in recovery, or, after death, at the most hyperæmia of the pia and the brain, or a permeation of these parts by serum was found in place of the supposed meningitis. After the true influenza period, Krannhals observed a number of cases which clinically resembled closely an undeveloped cerebrospinal meningitis, but which presented at the autopsy only excessive hyperæmia of the pia, without true inflammatory changes, and without the presence of bacteria; in every case there was pneumonic infiltration of the lower lobes of the lung. It is of extreme importance to remember that we may have these marked meningitic symptoms, such as great fever, apathy, sopor, stiffness of the neck, strabismus, inequality of the pupils, grinding of the teeth, hyperæsthesia, bradycardia, and intermittent respiration, without any lesions whatever of meningitis.

Spinal-Cord Affections.

In judging of the spinal-cord symptoms in influenza the same difficulties are met with which have been variously touched upon in the preceding sections. Here also the functional disturbances play so great a rôle that we are often led to assume the presence of a certain disease of the spinal cord, which diagnosis is upset by the further course of the affection. Reports concerning actual lesions of the spinal cord in influenza are exceedingly scarce when compared to the great number of clinical observations of spinal-cord affections.

In the section on functional nervous disturbances many cases were mentioned which could be repeated here. Benno Herzog has described cases whose symptoms he refers to a disseminated myelitis, which at first presented the picture of the so-called spastic spinal paralysis.

A girl, 8 years of age, was taken ill with influenza in the early part of February, complaining of violent neuralgia and cephalalgia. Three weeks after the beginning of her illness the parents noticed a paralysis of both legs, and this paralysis remained stationary while the general condition improved. While lying down, the patient could move the limbs only very slightly; on attempting to stand, which was impossible, the patient complained of pain in the soles of the feet and in the ankle-joints. No urinary or intestinal symptoms were present. In April, exaggerated triceps reflexes were noticed in the upper extremities, and the muscles of the lower extremities were somewhat firmer than normal. When lying down some slight mobility was present, but the patient was unable to walk. When an attempt was made to carry out passive motion, frequent contractions occurred in the left leg, and on the right side scarcely any passive movement could be made. When the patellar tendon was percussed, the legs were thrown into clonic spasms. If the patient was raised by the axillæ, the legs hung dangling, flexed at the hips. There were no disturbance of sensibility, no pain in the peripheral nerves, and no swelling of the extremities.

Revilliod reports a case in which a young girl, who had had a slight weakness of the legs during a primary attack of influenza, was taken with a total paraplegia, with symptoms of spastic spinal paralysis, after a relapse. Improvement was very slow.

Fiessinger reports under the name of myélite grippale the case of a boy, 14 years of age, who had a weakness of the legs accompanied by paræsthesia and dull pains five weeks after an attack of influenza. Then there suddenly occurred a total paraplegia with loss of the patellar reflexes and of sensibility as high up as the fifth intercostal space. Constipation, paralysis of the bladder, continued erections,

fever, and lancinating pains in the arms also existed. A few days later the limit of anæsthesia had extended to the third intercostal space, the neck became stiff, the arms were paralyzed, and respiration was labored. At this time trophic symptoms also appeared. After a week the symptoms improved, the fever, paralysis of the arms, and stiffness of the neck disappeared, but the legs, bladder, and rectum remained paralyzed, the integument of the legs was still anæsthetic, and the muscles were atrophied.

The typical symptom complex of Brown-Séquard's paralysis (hemiparaplegia with hemianæsthesia of the opposite side) was observed by Determann in a man twenty-five years of age immediately after an attack of influenza. Improvement occurred in the course of a few weeks, and Determann assumed that the symptoms had been caused by capillary hemorrhages and hyperæmia of the tissues of the spinal cord. Eulenburg reports a similar case of Brown-Séquard's paralysis following influenza in a patient seventeen years of age. Leyden mentions a case in a child of encephalomyelitis accompanied by acute ataxia, which ran a favorable course. Of other system diseases we may mention the following: polioencephalitis superior et inferior and poliomyelitis anterior, described by Goldflamm; acute ascending so-called Landry's paralysis, described by Féréol and Laveran; poliomyelitis acuta anterior (Teissier, Henoch, and Drashe). We observe in all these reports the extraordinarily polymorphous character of the lesions produced by influenza. The irregularity and variety of symptoms and the difficulty of interpreting them correctly are shown very strikingly in an observation of Leichtenstern, in which a woman, forty-nine years of age, presented the following symptoms as an immediate sequel of influenza: girdle pains and pains in the lower extremities, weakness of the latter with distinct ataxic symptoms, a normal pupil, total paralysis of the bladder, cystitis, no loss of sensibility whatever, enormous exaggeration of the patellar reflexes, and violent foot-clonus. This case resulted in recovery. This symptom complex, as Leichtenstern remarks, is one which corresponds neither to the picture of a peripheral neuritis following tabes nor to that of a spastic spinal paralysis or of a myelitis transversa.

Psychoses.

Among the great number of symptoms of involvement of the nervous system in influenza, those which have been mentioned above under hysteria and neurasthenia lead us imperceptibly to the psychoses. The extreme malaise and debility in influenza contain a hint of mental disturbances. There is no doubt that some nerve disturbances are fitted by their intensity to pave the way for mental affections. Thus,

the headache may for example become so intense or insomnia so persistent that through this alone mental irritability may be brought on. If we add delirium to these symptoms, we may comprehend that many physicians look upon psychic disturbances in influenza as very common. Others, however, have maintained the contrary. It is probable that this difference in opinion depends chiefly upon the question whether the appearance of the psychoses of influenza presupposes a congenital or acquired psychopathic condition, the influenza accordingly occupying only the rôle of an exciting cause, or whether influenza directly causes morbid psychological conditions in hitherto healthy individuals having apparently no predisposition to mental disease. It has been asserted by some who lived through the late epidemics, and who also distinctly recollected former ones, that the recent epidemics were distinguished by a peculiar prominence of the nervous and psychic affections. In a study on the psychoses of influenza, Althaus asks whether the psychoses following influenza occur more frequently than those which make their appearance after other acute diseases. In a certain sense this question has been answered affirmatively. Many observers have noted more cases of post-grippal psychoses during the last few years than of other post-febrile mental diseases during their whole lifetime, and psychoses following influenza are undoubtedly much more frequent than those occurring as a sequel to other infectious diseases. This might possibly be explained at first sight by the fact that grippe makes its appearance more frequently in the form of a pandemic than as an epidemic, and we might assume that mental disturbances occur more frequently in grippe because so many more persons are attacked by this than by other febrile diseases. If we compare it, however, more carefully with other infectious diseases, we shall be convinced that the poison of grippe exerts a more deleterious influence on the tissues of the brain than other toxins. Jastrowitz, in his report on psychoses in the German collective investigation, defends the impression that these conditions make their appearance not only absolutely, but also relatively more frequently after grippe than after other febrile affections. The only acute disease, according to Althaus, which can be compared with influenza in this respect is typhoid fever.

It has been pretty generally asserted that grippe alone is not capable of producing psychic disturbances and that if these should be developed, a congenital or acquired neurotic tendency must have existed in these patients. This opinion is held by Kraepelin and Ladame, also by Leledy, Van Deventer, and Bidou. Althaus, however, after a careful perusal of the published histories, finds that a predisposition was manifested in only 62.8 per cent., and none in

37.2 per cent. of the cases. Although, therefore, a predisposition may be an important factor in the occurrence of these psychoses, it is by no means the only one. This much is at any rate positive, that the gravity and duration of the psychoses are unfavorably influenced by the predisposition. That we may gain an insight into the peculiar influence of grippe on the mind, it is practical to adhere to the description of Kirn, who divides the psychic disturbances which occur in the course of acute febrile affections into two natural groups, according to the time of their commencement: (1) Those occurring during the febrile stage, and (2) those occurring after the fever has run its course.

The febrile psychic disturbances are by no means infrequently observed in influenza; they often present themselves most commonly in the form of febrile delirium, much more rarely as psychoses of long duration. The delirium, which is often compared with the analogous symptoms in typhoid fever, makes its appearance particularly in cases in which other cerebral disturbances are also prominent, such as stupor and clouding of the mind, hyperæsthesia, etc. They are generally combined with states of excitation or depression of short duration.

According to Kirn these are to be described as acute transitory psychoses, for the reason that, especially in influenza, we are able to observe the gradual transition of this delirium into those conditions which are recognized generally as true psychoses. Attention was drawn to this especially by the striking manner of its appearance, frequently it comes on when the patient feels perfectly comfortable and when no other symptoms of disease are present. On the other hand, it frequently accompanies those forms of grippe which are complicated by pneumonia. In this case, it may be distinguished from the delirium of common pneumonia, in that it stands in no relation to the extent of the lung affection, that it may make its appearance at the beginning of the disease instead of at its height, and that it is dynamic in character. The delirium of grippe may in fact precede all other local symptoms, it may follow them, or alternate with them, and especially with other cerebral symptoms. Hallucinations and sensory illusions, combined with motor excitement, give to this delirium its special stamp. It may be quiet and manifested by incoherent speech or may be noisy and find expression in loud screaming or lamentation. In many cases the delirium is combined with the patient's unconsciousness of his condition, while in other cases the patient retains in a measure his senses, and makes unsuccessful attempts to overcome his illusions and hallucinations. The latter occasionally present a remittent or intermittent type, thus running

their course, so to speak, in a number of paroxysms. This delirium is frequently met with in children, in individuals at the age of puberty, and also in those disposed to mental disturbance, especially habitual drunkards. Jastrowitz concludes, from the result of the collective investigation, that this delirium was characterized during the last epidemic of influenza not only by its frequent occurrence, but also by its independence. It is not solely a fever symptom, as it occurs not only during the latter but also after it has disappeared. Physicians have in many cases observed violent delirium and conditions of excitement accompanied by hallucinations, in a perfectly afebrile condition. The numerous hallucinations which make their appearance in delirium may involve all the senses, even those of smell and taste. Thus, some patients complain of anosmia, later of some especially disagreeable odor. The hallucinations may continue during the afebrile state, no other symptoms of delirium being present. Delirium potatorum, a form of delirium tremens, usually made its appearance during pneumonia and proved to be extremely dangerous to the patient. It is mentioned that delirium, lasting three days, always occurring towards evening, was present in one case.

In explanation of this delirium Althaus says that not only does the increased degree of fever exert its influence on the functions of the cerebral cells, inasmuch as increased heat always causes an irritation of nerve tissue, but that increase of the cardiac function, by promoting active hyperæmia of the brain, also contributes to the appearance of symptoms of irritation. This hyperæmia not only produces headache, insomnia, congestion of the veins of the choroid, and increased sensitiveness of the nerves, but clinically it is also related to the condition of unconsciousness, which may be followed by maniacal excitement and delirium, occasionally ending in coma and death.

According to Kirn, the febrile psychoses of influenza follow febrile delirium intimately, having no dividing line between them. Such a transition case is reported by Ewald. A boy seven years of age had gone to school in perfect health; after school hours, however, he did not return home as usual, but went to the railway station, saying that he was going to Leipsic. As he was unable to give an account of himself, he was taken into custody, and his identity having been established, he was taken home. Arriving here he was unable to recognize either his home or his surroundings. He continued for a few days longer in this condition, a victim of delirium which proved to be an initial symptom of influenza. This psychosis, however, appears more frequently on the second or third day of the disease than during its initial stage, and continues for a longer or shorter period

after the fever has ceased, to end usually in rapid recovery after one or more weeks. In this group of psychoses should be included those in which Leichtenstern says that he had the patients committed to an insane asylum, on account of the danger of their committing suicide or because of their turbulency, but that he was sorry later on that he did not allow them to remain at home, as they all rapidly recovered. In these psychoses the patient leads a perfect dream-life, unable to recognize his own position and surroundings. His moods are variable, although as a rule the depressing forms predominate, accompanied occasionally by apprehensions. Motility is as a rule increased as manifested by mimicry, gesticulation, restlessness of the legs in walking, etc. There are also increased speech movements, as shown by rapid talking, screaming, singing, and praying. Sensory delusions are as a rule present here. Sleep is greatly disturbed, being frequently absent altogether. The disappearance of excitement with a return of consciousness is usually rapid, accompanied by amnesia or only a general remembrance of the events of the attack. The prognosis of the febrile influenza psychosis may be considered favorable, as a rule. If death occurred, this was generally due to a complicating pneumonia or heart failure. Jastrowitz explains the acute confusion present in the first instance as only a protracted delirium, and sees the reason of its presence in the nervous disposition as well as in the strength of the influenza poison, which has acted on the psychic cerebral centres, so that this being the case, individuals not predisposed, as for example robust country people, are also attacked by it.

The post-febrile psychoses consist in those disturbances which make their appearance after the cessation of the fever. The time at which they appear is extraordinarily variable. This time is of interest in so far as the question might be raised whether we can still ascribe to influenza a mental disturbance which makes its appearance, for example, two to three months after the febrile affection. It seems to me that we are justified in this assumption, if for no other reason, because the disturbance of the equilibrium can be found at this time. Althaus concludes: (1) The psychoses which assume the form of maniacal excitement follow the attack quickly, usually making their appearance immediately after the crisis; (2) when the affection has the character of depression and melancholia it occurs somewhat later, namely, within a few days to a few weeks after the influenza; (3) a general paralysis may occur much later still, namely, as long as six months after the attack. Mispelbaum, who has written an excellent dissertation on the psychoses of influenza under Pelmann's direction, mentions the time as being usually four to six weeks, although in two

cases it was about fourteen days; Van Deventer places their occurrence eight, ten, twelve, or fourteen days after the influenza fever. As the post-febrile do not present the same simplicity of form as the febrile psychoses, Kirn has made various subdivisions, namely: (1) acute conditions of exhaustion; (2) melancholic conditions; (3) maniacal conditions. The acute exhaustive conditions which were first designated by Hermann Weber and Krepelin as asthenic psychoses are somewhat similar to the mental disturbances which make their appearance after pneumonia, after acute exanthemata, and during the puerperal period. They are characterized by rapidly developing acute conditions of excitement with innumerable delusions of the senses, in which an apprehensive, more rarely an expansive mood predominates. The illusions relate more to a feeling of depression than to one of exaltation. Developed in a higher degree, these disturbances have been denominated hallucinatory confusion. Kirn mentions as particularly characteristic of this form of the disease the condition of great physical weakness and anæmia, accompanied by a relatively slow return of strength. This bodily exhaustion may lead to a fatal termination. On the other hand, perfect recovery may, however, take place, even after relapses of this psychic confusion. The fact is also emphasized in Pelmann's cases that in the time between the attack of influenza and the beginning of the psychosis, the patients, though believing themselves free from the grippe, still have a feeling of debility, and unanimously complain of insomnia. In his cases the advent of the psychosis was always announced by an acute delirium, the "delirium decremente" of Weber, which lasted a few days (in one case two weeks), passing, except in two cases, into a melancholia of varying duration, never less than half a month. Pelmann is also of the opinion that the condition of general debility caused by the influenza is the principal factor in the injury to the cerebral functions, and therefore recommends that this period of exhaustion be most carefully watched.

The second group in Kirn's table includes the melancholic conditions. Their advent is particularly marked by a feeling of debility and of physical exhaustion.

This easily explained condition of depression may progress through all stages, until it reaches pronounced melancholia. This latter, following influenza, is in many cases a simple one, with perfectly retained consciousness, and frequently remains stationary at this low stage, taking on a hypochondriacal character, owing to the existence of numerous paræsthesiæ. In other cases the melancholia will increase to great apprehension, expressions of despair, suicidal impulses, and occasionally cataleptic symptoms. If delirium has preceded this melancholic condition, it is probably correctly looked

upon as a delirium of exhaustion. Kraepelin has mentioned cases of marked hypochondriasis, occurring, however, in those disposed to it and in otherwise complicated cases. The melancholic condition occasionally also is found in individuals who were dejected in spirit even before the attack of influenza. The third form of mania, which makes its appearance in the stage following influenza, is in all probability more rare than any other. Maniacal excitement usually develops about one week after the attack of influenza, and rapidly rises to its full height. As a rule we find simple typical mania, without the presence of hallucinations. Where raised self-esteem is present we usually note a serene temper, and excitement in all motor areas, more rarely an irritable temper and discontent. A characteristic quality does not seem to be possessed by these manias, however. Most cases may be treated at home, and end in recovery.

The majority of authors are as adverse to the idea of a peculiar grippe psychosis, as they are to admitting the existence of a special typhoid or puerperal psychosis. Althaus, however, mentions cases of general paralysis after grippe in which no predisposition was present, and points out that the melancholic delirium of grippe is not a peculiar kind, but that it also occurs after typhoid fever and acute articular rheumatism. He takes it for granted that the most frequent form of the disease is that of an acute hypochondriacal melancholia, as 41.2 per cent. of all patients suffered from this. Aside from the forms described here Kirn mentions another group under the title of pseudogrippal psychoses. These represent individual hysterical and paralytic disturbances, as well as a few cases of paranoia. They are to be explained by the assumption that the diseased conditions were present before the advent of the influenza, but became developed to such a degree that they were evident even to the laity as a result of the shock of the illness. In the collective investigation reports acute paranoia was only rarely mentioned. A weak memory is noted with remarkable frequency in grippe, especially after the disappearance of the primary trouble. This can only be looked upon frequently as a symptom of exhaustion. Jastrowitz seems inclined to place cases of aphasia in influenza here, and to refer the condition to a weakness of the word-memory. A couple of observations of Henius in Berlin, however, point to the fact that here as elsewhere the injury of the brain by the poison of influenza is a more constant factor in the functional cerebral disturbance than is exhaustion. The patients were two women in whom there was a nearly total abeyance of the psychic functions. One of them was a very old, but mentally and bodily still vigorous lady; her memory suddenly left her altogether and she was unable to recollect the day of the month or the year, but

was perfectly aware of her loss of memory. After thirty hours memory again returned. The other patient, a domestic twenty-three years of age, was unable to perform any work, remembered nothing that was told her, could not sleep, and complained of severe headache, but she had no fever; by the end of a week she had recovered perfectly. An interesting case of aphasia was observed in an artist, who became ill with a violent catarrh and fever, which was followed by total aphasia; the young man could understand everything that was said to him, was himself, however, not able to utter a word. In twenty-four hours the power of speech was again restored.

As regards influenza in the insane, these persons are not more frequently attacked than the healthy, neither are there any peculiar symptoms in them, although in the reports of certain individual institutions a temporary aggravation of the mental malady was noted.

Diabetes insipidus has been met with in a few cases after influenza as a peculiar symptom, showing an involvement of the nervous system.

Circulatory System.

The bacilli of influenza do not permanently make their home in the *blood*, and they have been only temporarily and rarely met with here. This fact has caused astonishment from the beginning, for the reason that it was thought the varied clinical symptoms of influenza, the polymorphism of the disease picture, could be best explained by a dissemination of the bacilli through the blood. Besides this, many symptoms on the part of the circulatory organs were so striking that these also seemed to point to a disease of the blood itself. It has been mentioned above that slight symptoms of icterus were thought to point to changes in the composition of the blood, and that, in the examination of urine, elements were looked for which could be referred to disintegration of the blood. No sufficient ground was obtained in all these studies to assume the existence of blood changes such as we meet with in septic diseases. It goes without saying that the secondary affections, which are disseminated by means of the blood current, are not here included.

The experiments made to determine the action of the blood in influenza have not given the same results in all cases. While some, as von Jaksch, deny that blood changes occur, others admit of slight changes. Thus Klebs assumes that there is a slight decrease of the red blood corpuscles, and Přibram a diminution of hæmoglobin during the period of convalescence. A still more marked diminution of the red blood corpuscles and of the amount of hæmoglobin has been claimed by Schirmer, whose statements are corroborated by Renzi.

Other changes in the blood were assumed by Bäumler, who noticed a remarkably large number of degenerated corpuscles. Klebs attributes great importance to the appearance of granular masses in the blood. He looks upon these as derived from degenerated red and white corpuscles. All this is in accord with his belief that the most important changes of influenza occur in the blood itself. He carried this opinion so far that he even considered the seemingly primary catarrhal and inflammatory symptoms as the result of the occlusion of large capillary areas by the thrombi, resulting in hyperæmia, inflammation and exudation, deposition of pathogenic microorganisms, and the preparing of a suitable soil for the development of the latter. He believes that the nervous symptoms are caused by these circulatory disturbances, the influence of the toxins being very subordinate. Bäumler rested his assumption that in influenza grave changes occur in the blood on the great decrease of hæmoglobin, and he regarded as related to this the frequent appearance of icterus, urobilinuria, and hæmoglobinuria. It must be admitted, however, that the changes above described are not constantly present, and we believe that while they may perhaps be employed for a partial explanation of the changes occurring in influenza, they by no means make the assumption of a specific influenza toxin necessary. The fact that the spleen is so frequently found enlarged in influenza is an argument in favor of the occurrence of marked blood changes. An increase of the white blood corpuscles also in uncomplicated cases of influenza has been observed by numerous investigators; on the other hand, a true leukæmia or even an acute pernicious anæmia has been observed only very exceptionally in influenza.

The *cardiac* symptoms are of great importance, as they serve to distinguish the picture of influenza in a peculiar manner from that of other infectious diseases, and because also in the greater number of cases the true cause of death is to be found in an affection of the heart. The extremely rapid pulse has been noticed from the beginning by all observers; it is present in influenza whether fever exists or not, and is by no means proportionate to the increase in temperature. It is usually an expression of the great physical debility; it is rarely tense, more frequently small and weak; a pulse of 100 to 120 is not rare, even in the absence of fever. This condition of the pulse has been found also when other inflammatory affections could be demonstrated. In ordinary non-grippal pneumonia we usually find a special form of pulse which was formerly designated a pulse of inflammation, and a certain relation usually exists between the pulse and bodily temperature, but the pulse in the pneumonia of influenza retains the qualities of the influenza pulse. It is rapid, soft, easily

compressible. In the pneumonic affections of influenza this condition of the pulse has frequently puzzled us, because we are used to look on a pulse rate of 120 and over as a very unfavorable symptom in a simple pneumonia. This tachycardia, however, is not invariable in influenza, for we meet occasionally with cases of bradycardia, or marked slowing of the pulse. This peculiarity seems to have been observed in a varying frequency in different localities, for it is considered by some observers as especially characteristic of influenza, being observed more frequently here than in any other acute infectious disease. It was mentioned in the accounts of epidemics during the last century, and was observed in that of 1889-90. It seems to have occurred with particular frequency in Munich, where among 275 patients 46 per cent. showed a marked slowing of the pulse, either an absolute slowing if the rate is 40 to 60 beats in an afebrile course, or a relative one if there are 60 to 120 pulsations during high fever. Leichtenstern has observed 106 pulsations to the minute in a case of influenza pneumonia with a temperature of 40.7° (105.2°), and only 94 accompanying a fever of 39.3° (102.7°), showing that this functional anomaly attributed to influenza occurs even during pneumonia. Other anomalies of the heart's action are presented in the irregularity of the pulse, and in the great variation of the pulse rate; it may rise from 80 to 130 beats, when the patient changes from the recumbent to the sitting posture, the *pouls instable* of Huchard.

Leichtenstern also describes a peculiar variation in frequency, which is recognized in the changed rate during succeeding quarter minutes, and which he designates alloiorrhythm or poikilorrhythm. The strong action of the poison on the heart early leads to the appearance of the dicrotic pulse, to which Přibram has especially drawn attention. It cannot be denied that nervous functional disturbances are at the bottom of these forms of the pulse, and they oftentimes also are accompanied by other symptoms, for example by a feeling of distress in breathing, pain in the region of the heart, precordial distress, lancinating pains in the side, so that these cases may present the picture of a true neurosis of the heart. All these symptoms occur along the line of heart failure, and death in truth has happened in consequence of a sudden cardiac paralysis in the beginning of influenza or even during convalescence, no gross changes of the heart muscle being found. Cardiac debility is also supposed to be an explanation for the occurrence of glaucoma, by Sattler, Ebersbusch, and Knies. This action is especially noticeable in cases in which the heart is already abnormal. Thus we have seen many cases of autopsy, in which there was some preëxisting affection of the heart, such as simple valvular disease, which, in the absence of

the attack of influenza, would probably have gone on without serious result for a long time. In other cases complicated valvular affections suddenly made their appearance in cases of preëxisting Graves' disease.

Of truly inflammatory diseases pericarditis and endocarditis are observed in influenza; the former is usually of the dry form, but serous and fibrinous exudates may also make their appearance. Of endocarditis it is said in the collective investigation that it had always appeared in that varicose form are which is found on the free borders of the valve, on the side facing the blood current and accompanying, as we know this form does, numerous acute diseases. Pericarditis was in all probability most frequently a sequel in cases in which pneumonia, pleuritis, or articular rheumatism was present. The endarteritis seems to present only in very rare instances an ulcerative character, perhaps only when a previous disease was forced by the influenza into an ulcerative stage. That these cases are frequently due to a mixed infection can be proved by the fact that Oulmont and Barbier have demonstrated the presence of streptococci in the valvular vegetations. The myocarditic affections in influenza are also to be looked upon usually as complications in the mixed infection of influenza. Myocarditic changes and parenchymatous and fatty degeneration of the cardiac muscle have been demonstrated in these cases, accompanied by consecutive dilatation of the ventricles. Lenhartz, in a case of influenza pneumonia complicated by pleuritis and pericarditis, found small metastatic abscesses in the cardiac muscles which contained streptococci. These myocarditic affections do not often occur, but are frequently brought to mind when irregularity of the pulse is found in influenza. If this irregularity remain for a long time after the disappearance of the influenza, it can be differentiated from myocarditis by the fact that the irregularity existing without great circulatory disturbances gives the impression rather of a neuropathic anomaly than of a sequel due to degenerative inflammatory processes.

The *blood-vessels* have been found greatly changed in influenza. On the part of the venous system, phlebitis and thrombosis frequently make their appearance during the period of convalescence. According to the report of the collective investigation committee disease of the femoral vein was with few exceptions present, much more rarely than that of the anterior tibial and brachial. The cases were not often fatal; twice death was due to hemorrhagic infarction of the lung, in one instance it occurred as a result of amputation of the thigh for gangrene. It is very likely that the involvement of the veins of the lower extremities may be due especially to cardiac de-

bility. Leichtenstern regards the fact that this change may be of a very acute character as a special peculiarity of this venous thrombosis. He reports a case of thrombosis of the veins of the arm occurring in a robust physician, and accompanying a severe cardiac influenza, which led to a marked swelling and a blue discoloration of the whole extremity within twenty-four hours. He refers the fact that gangrene has been observed in cases of thrombosis of the veins to this obstructive change. As this occurs so very rarely, Litten believes that in a case reported by the collective investigation, the gangrene of the thigh had probably been erroneously referred to a venous thrombosis. According to Leichtenstern, however, it is repeatedly mentioned in the history of the disease that the arteries are not occluded in these cases, but that, on the other hand, the venous thrombosis leads to grave changes in the extremity affected. We may mention an observation of Johannsen as belonging here, which relates to a thrombosis of the veins of the right arm and of the right lower extremity; at the amputation of the thigh for gangrene, all of the veins were found to be filled with deeply extending, firm thromboses; the femoral artery, on the other hand, was the seat simply of atheromatous degeneration.

In influenza we meet with a spontaneous thrombosis of the arteries such as has been regarded by Virchow as marantic and which has been met with hitherto chiefly in the course of typhoid fever. One of the first cases of this kind was described by Leyden. It has its seat by preference in the popliteal artery and makes its appearance most frequently during the period of convalescence. This accident leads to a grave condition of gangrene of the lower extremities, which has been described by Eichhorst, Gerhardt, and Cammerer, and which occurred not only in aged and decrepit individuals, but also in the young and robust. Occlusion of the arteries, like thrombosis of the veins, occurs symmetrically, involving the corresponding vessels on the two sides. The symptoms of an arterial occlusion in influenza do not differ from those of the similar condition occurring at other times, and consist in a sensation of cold and anæsthesia of the extremities, absence of the pulse beat, occasionally violent pain, bluish-black discoloration, and mummification of the parts involved. The prognosis is unfavorable, death occurring usually even after amputation. Septic symptoms of a general kind frequently make their appearance after arterial thrombosis. In the German collective investigation report eight cases of arterial thrombosis are mentioned. Four of these were unilateral, involving the popliteal artery; the fifth, which was also in the popliteal artery, was accompanied by symmetrical gangrene of both legs; the sixth case was one of thrombosis of the

femoral artery with gangrene; the seventh thrombosis of the brachial artery, and the eighth thrombosis of the cerebral arteries. In addition to this, occlusion of the arteria centralis retinæ and of the arteria fossæ Sylvii was observed, but the condition in these cases was due to an embolic closure of the vessels accompanying chronic endocarditis.

As to the cause of these thromboses, we must of course bear in mind that in degenerative disease of the cardiac muscle the formation of a thrombus occurs in the right as well as in the left ventricle, as has been frequently demonstrated post mortem. Besides this, emboli will be disseminated by an acute or chronic endocarditis, or arteriosclerosis of the aorta may be the cause of the formation of thrombi.

In other cases, the already existing senile changes will be so aggravated by the influenza that the formation of thrombi can take place. Primary or spontaneous arterial thrombosis is dependent, von Leyden is inclined to think, upon disintegration of the white blood elements; this increases progressively from the commencement of the disease to the crisis and also beyond it. Thus we must place these thrombi formations in a line with the action of blood-plaque thromboses in various cases of poisoning (phosphorus, chlorate of potash); possibly an extraordinary spasm of the vessels may also play a rôle here, as is assumed by Gerhardt. This becomes plausible by the observations made on the spasmodic action of the peripheral blood-vessels, as described especially by Petrina, who noted the occurrence of temporary changes in temperature from cold to warm of a finger or a toe, in the course of influenza.

The *hemorrhagic* symptoms in influenza, which are the evidence of intense impression of the poison of influenza on the blood-vessels, are in a high degree interesting. Attention has already been drawn to hemorrhagic encephalitis in speaking of cerebral diseases; large and small hemorrhages are of not very infrequent occurrence in this organ. But we also meet with a great variety of hemorrhages in other parts. Pick has described a case, which ran a rapid, short course, under the picture of a hemorrhagic diathesis. Bleeding from the nose, chiefly in young individuals, has been frequently observed, and described especially by Peiper; in other recorded cases violent epistaxis has occurred only late in the course of influenza. The sputum frequently presents an admixture of blood in the shape of streaks and dots, and true hemorrhage of the lungs has not infrequently been observed, even in the absence of tuberculosis. I have seen violent attacks of hæmoptysis in some cases of chronic pneumonia, occurring at long intervals; and in another case, bronchial hemor-

rhage has now lasted about four years, almost without cessation. Hemorrhages into the skin in the form of petechiæ have been repeatedly described, and also hemorrhages of the tympanum and the frequent admixture of blood in the purulent exudation from the ear, are recorded. Brando mentions three cases in which such hemorrhages occurred in the absence of otitis media.

Helling twice met with an initial hæmatemesis in cases in which no suspicion of gastric ulcer was present. Intestinal hemorrhages occurring in otherwise healthy individuals after an attack of influenza have also been reported. As a rule, these bloody evacuations continued for a few days, and were then followed by mucous stools. Keilmann and Dietrich described these in the gastric form of influenza. Cases of hemorrhage from the kidneys in the form of hæmaturia have been described by Eichhorst, or in the form of hæmoglobinuria by Bäumler; slighter admixtures of blood in the urine were found in some cases of nephritis. The menstrual flow during the attack of influenza has in many instances been reported to be more violent than usual and of longer duration. Haken observed violent metrorrhagia in certain cases in which no tendency to hemorrhages of this sort had been formerly present, and Helling observed in a woman forty-nine years of age, who had ceased to menstruate for five years and who had no uterine disease, a hemorrhage from the uterus during an attack of influenza.

The Skin.

The symptoms of the blood-vessels, described above, now lead us on, by way of the hemorrhages and the vasomotor functional disturbances, to the lesions of the skin observed in influenza. Just as spasmodic affections occur in the smaller vessels, so may paralysis take place in them. It is of very common observation in influenza to find the skin of the face reddened and swollen, so that we are probably justified in assuming a paralysis of the vessels as the cause of this symptom. The redness of the skin in many cases spreads far beyond the face over the whole body. This eruption is usually not uniform, but occurs in spots, and then presents an appearance similar to the exanthem of measles or of scarlet fever. French investigators have described especial varieties under the names of scarlatiniform and rubeolic (Teissier), which are in fact frequently quite difficult to distinguish from true measles and scarlet fever. This exanthem often reminds one of that which is caused by antipyrin, but it occurs in cases in which no antipyrin has been used. The eruption generally occurs during the febrile stage, and when, as frequently happens,

there is at the same time a marked hyperæmia of the conjunctivæ or painful affections of the throat exist, the similarity to measles or scarlet fever becomes even more remarkable. A special eruption peculiar to influenza has not been observed. A peculiar eruption which was described by Aman probably belongs, as Bäumler thinks, to the metastatic eruptions in septicopyæmic conditions. Schwimmer has described a polymorphous erythema exudativum. Hoffmann observed in two hundred cases of influenza five cases of an exanthem, among them two of very pronounced erythema. The forms under which these eruptions appear are, in addition to those mentioned, urticarial, herpetic, and erysipelatous. The urticarial eruption is frequently found among the other forms. A case of urticaria pigmentosa occurring in the course of influenza has been reported by Teubner. The morbilliform and urticarial eruptions are extraordinarily evanescent, as are also the general redness of the skin, the rarely encountered roseola-like exanthem, and a macular one which resembles that of typhus fever. Of somewhat longer duration are the herpetic eruptions. These occur as herpes labialis, or on the face, the nose, or the eyes. The members of the German collective investigation committee noted the occurrence of herpes facialis or labialis in six per cent. of their cases. Among the skin-affections which Schwimmer described, the herpetic forms were also the most frequent; he met with herpes iris and circinatus in two cases. Leichtenstern observed herpes in four per cent. of his cases, and that somewhat more frequently in those which were complicated by a pneumonia. Herpes of the tongue has occasionally been mentioned. Herpes zoster also occurs, sometimes on the chest accompanying intercostal neuralgia, in a few cases in the region of the supraorbital nerve, and also in that of the sciatic. Hoffmann mentions a case of herpes in which the whole left side of the face between the lower eyelid and the upper lip, also a part of the lip itself, was covered with groups of vesicles. These forms have usually been observed during the decline of the influenza attack, but a few cases of urticaria eruption and herpes zoster have occurred as late as fourteen days after the cessation of the disease, so that we may designate them as late exanthemata. Krannhals also most frequently observed herpes of the face, more rarely of the trunk and the extremities. As a curiosity we may mention the unique case in which, after the cessation of the fever, an intense scarlatiniform exanthem appeared; it was strictly symmetrical, confined to both legs and forearms, and was accompanied by great itching; it lasted five days. Erysipelas is mentioned by 1.7 per cent. of the reporters in the collective investigation; it occurred during high fever. Miliary vesicles frequently occur, which is not strange in the presence of the tendency to profuse

sweating. Eczema has been observed in influenza, and fleeting œdema is also described.

General furunculosis of the skin has been rarely met with of late, but was frequently mentioned in former epidemics. Petechiæ and larger hemorrhages, also profuse effusions of blood under the skin, have been described. Many cases of hyperæsthesia of the skin point to an affection of the cutaneous nerves, which may become so severe that even the feeling of the pulse is painful. Itching of the skin, sometimes very severe in character, may be present and may persist for a long time. Alopecia areata is probably to be classed among the dermatoneuroses of influenza. It was observed in one case in a woman, thirty-five years of age, who had experienced severe cephalalgia while suffering with influenza. After the second attack the hair began to fall out, and bald spots began to develop within the areas of the supraorbital and occipital nerves. Later on the headache ceased, and the hair returned. In this category also, in all probability, belongs the case of vitiligo observed by Simson. Rapid turning gray of the hair of the scalp and of the eyelashes has been noted by Bossers and Bock. Here should be included extreme dryness of the skin, and also the opposite condition, a great tendency to sweating. The heavy sweats frequently make a diagnosis very difficult in influenza, when the latter is complicated by pneumonia or by affections of the joints and bones. These influenza sweats may be so severe as to lead us to suspect grave septic conditions, when they may be of no serious import whatever. I have seen a man who suffered for months after an attack of influenza from hyperidrosis, which nearly drove him frantic. When the man stood naked in a cool room, the perspiration would literally pour in streams from his skin. It is interesting to note that in this case atropine had no effect whatever, while the attacks suddenly disappeared after salipyrin was administered. As rare forms we may mention, pemphigus simplex and hæmorrhagicus, purpura hæmorrhagica, and impetigo folliculitis suppurativa.

The occurrence of skin eruptions in influenza has given rise to the belief that this disease is somehow related to dengue, and that we are dealing with either the same or at least a related affection. On the other hand we may mention that dengue, in its epidemic form, progresses much more gradually than does influenza, also that in dengue the articular affections present the most prominent symptoms. Although the skin eruptions of dengue may be absent in whole epidemics, the exanthem nevertheless occurs much more frequently in dengue than in influenza. Both diseases present a similarity in that the exanthem is of such a polymorphous character. The exanthem of dengue shows certain peculiarities; we meet here, for example,

with both initial and terminal varieties, either of which appears only in very isolated cases during influenza; together with this we find, after dengue has run its course, that in most cases an extensive desquamation occurs, during which, not infrequently, great adherent pieces of epidermis are thrown off.

Genitourinary System.

As a rule, affections of the kidneys are not of frequent occurrence in influenza, at any rate by no means so frequent as in scarlet fever, diphtheria, pneumonia, and other infectious processes. *Albuminuria* has frequently been observed; it may be referred to the fever, but many regard it as a symptom of special frequency in influenza. Senator met with it in 18 cases out of 52, Brandes in 23 cases out of 27, and Teissier in one half of all his cases. As a rule the albuminuria is only temporary. Leichtenstern is inclined to attribute the great difference in the reports on the frequency of albuminuria to the different manner of testing for albumin. A true nephritis seems to occur but rarely in influenza; Leyden, Mosler, Strümpell, Přibram, each report a case; the German army report contains only 10 cases of severe inflammation of kidney out of a total of 55,263. Leichtenstern found only 2 cases of acute hemorrhagic nephritis in 439 patients. Anatomically a simple parenchymatous degeneration or glomerulonephritis has been found (Wallis, Weichselbaum, Ribbert); the necrotic processes which have been described by Beneke and Kuskow are in all probabilty to be referred to mixed infection.

One of the first cases of nephritis due to influenza was recorded by Leyden, who demonstrated the lesions of an acute nephritis in microscopical sections of the kidney of a woman who had died during an attack of influenza. The patient was a seamstress, 25 years of age, who, being previously in perfect health, was taken ill early in December with influenza. She complained of violent headache, to which was added slight difficulty of hearing, and since then she had never been perfectly well. She became weak and miserable, lost her appetite, and was seized early in January with violent vomiting, lasting eight days. About this time the patient observed that her urine was becoming scanty and turbid; at the same time œdema made its appearance. On February 8th she died. No special local phenomena were present, neither was otitis severe; moderate deafness existed, but there was no fever. The most important symptom was a great diminution in the quantity of urine, so that the daily excretion did not exceed 200 c.c. The urine was bloody and contained a large quantity of albumin, as is usually the case in acute infectious nephritis. Towards the end of January some improvement began to appear, the urine became more abundant, but in the mean time the strength of the patient had been so far undermined that she succumbed. At the autopsy, the kidneys were found enlarged and congested, therefore still in the

first stage of Bright's disease; on microscopical examination they also presented that form which we may designate as the most frequent typical form of nephritis, following acute infectious diseases, the type of which scarlatinal nephritis especially represents.

This form accords with that which, according to Klebs, is usually called glomerulonephritis or, better yet, capsulonephritis. Bowman's capsules are dilated and filled with numerous cells between the capsule and the glomeruli, and which compress the latter more or less. This explains the diminished secretion of urine. Leyden observed three cases of nephritis during this epidemic, two of which were complicated with pneumonia, and were both fatal. The case described above was interesting from the fact that there was no pneumonia nor was any localization of the infection to be discovered in the dead body, but the nephritis followed immediately after the otherwise anatomically unmarked influenza.

From the reports on the influenza in Bavaria, we learn that the kidneys not rarely became affected in influenza. The appearance of albuminuria was accompanied in a number of cases of influenza with very high fever. A number of observers in that country mention the occurrence of acute nephritis, frequently of a hemorrhagic variety. In several cases recovery took place within eight or nine days. One case was observed in which nephritis accompanied by hemorrhagic symptoms made its appearance on the fifth day of the disease. In Würtemberg cases of nephritis, as well as of other urinary disturbances, such as cystitis and hemorrhages from the bladder, were observed occasionally only; such was also the case in Baden.

Hæmaturia renalis was observed by Krannhals several times. In one case a fifteen-year-old lad was affected by it eight days after a short attack of influenza; it disappeared after rest in bed for four weeks, but reappeared at the end of six weeks, and then continued another six weeks.

A number of cases of *glycosuria* and *diabetes mellitus* have been reported. In some cases there was merely a temporary appearance of sugar in the urine, in others diabetes of longer duration. An unfavorable influence of the influenza on an existing diabetes has been pointed out by Kahler, Drashe, and Féréol.

Among the affections of the *bladder* have been described certain nervous disturbances which presented themselves under the forms of paresis of the bladder and retention of urine, spasms, and painful sensations in the bladder. True cystitis and hemorrhage of the bladder have only rarely been observed.

The action of influenza on the *genital organs* may in part have already been shown by the cases of hemorrhage from the uterus and

the changes occurring in menstruation, referred to above. As to its influence on pregnant women, we already know from former epidemics that abortion is frequently caused by it. Aman gives the histories of fourteen pregnant women who fell ill with pronounced symptoms of influenza. In six abortion occurred, and each of the remaining eight gave birth prematurely to a living child a few weeks before term, the labor pains coming on at the very beginning of febrile symptoms. The occurrence of abortion is also mentioned by Muller and Trossat, by Hertzsch and Huber. The fact that a general decrease of the birth-rate was observed in 1890 was looked upon as a result of the influenza epidemic. Bierner, Lvov, and Gottschalk refer the occurrence of abortion to the metrorrhagia which is also observed in the non-pregnant. Gottschalk assumes that an acute hemorrhagic inflammation of the decidua is occasioned by the influenza, in which view he is upheld by Viney.

Among affections of the male organs of generation we may mention an influenzal orchitis which has been observed a number of times. Kottmann mentions a case which went on to suppuration; others describe the occurrence of gangrene of the scrotum, gangrene of the penis, and periorchitis. Leichtenstern mentions that the English epidemics of influenza in 1732–33 and 1737–38 were marked by the frequency with which orchitis and inflammations of the parotid gland occurred as complications, which leads one to believe that possibly an epidemic of parotiditis went hand-in-hand with that of influenza.

The Bones and the Joints.

We need not here return to the appearance of muscular atrophies and of pain in the muscles, on account of what has already been said in discussing affections of the nerves and of the muscles. These are accompanied by contractures and by myositis, as well as by multiple muscular abscesses, caused by mixed infection, and by hemorrhage into the muscular tissue. The articular and bony system may be affected to a marked degree in influenza. This has been more fully described in a monograph by Witzel, who looks upon these affections as analogous to the articular disease which makes its appearance among horses in epidemics of epizoötic disease. Severe forms of disease of this kind have been observed even after the subsidence of the influenza epidemic.

Rheumatism of the joints and bones has been frequently met with, together with sensations of tearing and pulling in the limbs and along the spinal column. Multiple arthralgia also is not a very rare complication of influenza; it usually attacks the larger joints. We

are unable to tell how frequently true effusion occurs into the articulations in consequence of an irritation of synovial membranes. Witzel reports cases in which the articular inflammation caused particularly severe symptoms, or ended in chronic dropsy. He also describes more minutely the rheumatoid affection of the bones in influenza, which reminds one strongly of the similar affection occurring in typhoid fever and in gonorrhœa. He mentions one case occurring in a child in which this affection of the bones appeared where, during the attack of influenza, the bone had been contused; in others a slight enlargement of the tibia due to an old injury was present before the grippal affection settled there. In another case there was a periostitis of the lower half of the right thigh; the bone seemed as though surrounded by a tough, firm infiltration which was very sensitive to pressure. The treatment, which was followed by recovery, consisted chiefly in fixation. The same author mentions a case of suppuration of the knee-joint, the origin of which could be referred to an attack of influenza. Kroenlein and Walker also observed cases of acute purulent inflammation of the knee-joint, Moeser met with two cases of periostitis of the upper jaw, Boese with one case of periostitis purulenta of the tibia in a young and strong adult. Leichtenstern mentions a peculiar, very painful inflammation and thickening of the plantar fascia. I myself have repeatedly seen very painful affections of the fascia of the pectoral muscles and those of the thigh, after influenza, which were looked upon as rheumatic affections, and in which in many cases there developed in the painful region a great number of small nodules reaching the size of a pea. These affections were quite intractable, but the most favorable results were obtained by salicylic-acid preparations. I am convinced, therefore, that we were here dealing with inflammatory processes of the fasciæ. There are undoubtedly many cases of mixed infection in influenza which induce inflammatory changes in several joints at the same time. In how far the influenza is responsible for this we cannot say, but we may mention in this connection that we are in possession of some observations showing a marked aggravation of surgical diseases during influenza. Verneuil has arrived at the conclusion that grippe in its character as an infectious disease exerts a deleterious influence on injuries and surgical operations during the attack as well as during convalescence, and this is shown by a tendency to suppuration, so that we meet with suppuration in conditions in which, thanks to antisepsis, it is usually absent. Surgical diseases are also aggravated by the occurrence of phlebitis, arteritis, lymphangitis, etc. As a whole, the pyæmia of influenza seems to Verneuil to run a milder course clinically as well as anatomically than pyæmia does ordinarily.

Surgical measures are indicated in the suppurative localizations of grippe, but operations should be undertaken in patients who have suffered from influenza only if they are in a perfectly normal condition, and internal antiseptic medication should always be employed as a preparatory measure. Walker mentions the occurrence of grave suppurative processes in the bones and cases of perinephritis and pyelonephritis following influenza.

The Eyes.

Remarkable as is the variety of symptoms caused by grippal localizations in the different organs, the manifold phenomena which are referable to the affections of the eyes in the course of an influenza are yet more astonishing. These affections run from the slightest form of conjunctivitis to the very gravest of eye diseases, and hardly a tissue of the eyeball and its adnexa is exempt. The recent epidemics especially have taught us that, beside the great variation in gravity, a variation in the frequency of eye diseases occurs at different places. In many localities the eye affections were regarded as exceptional, in others as characteristic of influenza. A very interesting dissertation on the eye affections has been written by Hillmanns, under Saemisch of Bonn, which summarizes very clearly the eye complications of influenza and classifies them as follows: (1) Inflammatory symptoms; (2) symptoms referable to the nervous system; and (3) symptoms relating to the circulatory apparatus. Among the *inflammatory affections* those involving the palpebral conjunctiva, cornea, uveal tract, retina, and Tenon's capsule are the most frequent. The most common form of palpebral affection is an œdema of the lids and the formation of abscess. Œdema of the lids (Landolt) may occur with or without conjunctivitis. The first occurs more frequently in the period of convalescence, when the lids may very suddenly, for example during the night, become greatly swollen, and the skin present a rose tint, quite different from the redness caused by erysipelas. The affection is benign and runs a rapid course. Abscesses of the lids appear more frequently among the sequelæ and with its occurrence the temperature may again rise, the lids become œdematous, take on an erysipelatous hue, and pus forms in them. On incision fetid pus is evacuated; this affection is also benign, and heals within fourteen days if well incised and drained. The most frequently occurring affection is conjunctivitis, which makes its appearance in most cases as a simple catarrh, differing from it, according to Ebersbusch, only in that it develops more speedily, and also recedes more rapidly; it is accompanied by photo-

phobia, lacrymation, sometimes by a mucopurulent discharge; occasionally a true episcleritis is added. Gradenigo points out that this affection may also occur without a nasal catarrh, and furthermore, that the conjunctival changes, which occur nearly always during the stage of fever, also not infrequently make their appearance as a sequel or a complication, and finally that they accompany the often grave affections of the cornea and the conjunctiva. From New York also we hear of the occurrence of episcleritis in influenza. Wicherkiewicz reports cases of conjunctivitis which were especially remarkable for their intractability, and Althaus describes symptoms which occurred so frequently that he at first thought of the gonorrhœic form, in which small hemorrhages are also met with in the subconjunctival and episcleral tissue. Pflüger, on the other hand, observed hyperæmia of the conjunctiva in influenza, while true inflammations of this membrane were much more infrequent. In two cases the inflammation took on a fibrinous character; occasionally it also made its appearance in the form of catarrhal swellings and œdema of the lids, and eczematous inflammations likewise occurred.

The tear ducts also become affected, and in a few cases a unilateral, purulent dacryocystitis has been described, being distinguishable from the like idiopathic affection only by the unusually good results of daily irrigations. The direct extension of the process from the nose cannot be doubted here. According to the statistics of Saemisch we meet with two peculiarly rare forms of keratitis: namely, keratitis punctata superficialis and keratitis dendritica exulcerans, for the latter of which herpes corneæ febrilis is considered by him as a prodromal stage. Keratitis punctata preferably attacks youthful individuals, and usually involves both eyes. It is generally accompanied by a catarrh of the respiratory organs, and is ushered in by a violent catarrhal conjunctivitis with marked ciliary injection. As far as the etiology, seat, and sequence of the corneal infiltration are concerned, it is said to resemble herpes corneæ febrilis, which occurs especially in febrile diseases of the respiratory organs together with herpes nasolabialis. Keratitis dendritica exulcerans has been more minutely described by some other authors, especially by Eversbusch. The latter looks upon it as a herpes corneæ cachecticus, as this form is also met with in afebrile conditions, especially when there is lowering of the general nutrition, as in scrofula or tuberculosis, and also in the protracted convalescence of influenza.

The absence of pain and of symptoms of irritation, as well as the diminished sensitiveness of the cornea, is interesting in these cases. Adler, of Vienna, has observed unilateral punctate infiltrations of the cornea accompanied by hypopyon, also keratitis dendritica, after

severe attacks of influenza, also a keratitis parenchymatosa and finally perforation of an old ulcer of the cornea as a result of violent sneezing due to influenza. Most authors see in keratitis dendritica a developmental stage of the form of herpes above mentioned, caused by a necrosis of the covering of the herpes vesicle with loss of epithelium. Healing is here often delayed, linear opacities, etc., being formed. Among other affections of the cornea Pflüger observed a case of eczema racemosum; and Dente states that the corneal affections observed by him frequently took on a malignant character, rapidly leading to suppuration and disintegration.

One other exceedingly rare affection has been at times observed in influenza, namely, a primary tenonitis. Inflammation of Tenon's capsule is perhaps a cause of the frequently occurring pain in the eyes on movement; it must not be mistaken for secondary tenonitis, in which the inflammation proceeds from the globe; in the latter case the exudation is often of a plastic nature and leads to adhesions between the globe and wall of the capsule. Tenonitis occurring in influenza may be purulent, and has caused blindness in one case in consequence of the escape of pus from the capsule into the globe; in other cases a serous and fibrinous inflammation, accompanied by œdema of the lid, protrusion of the eyeball anteriorly, loss of motility, and œdema of the conjunctiva, was present. In these cases the symptoms receded after a few days. As regards the differential diagnosis between inflammation of Tenon's capsule and that of the orbital cellular tissue, emphasis must be laid on the normal ophthalmoscopic findings in those cases in which a suppurative tenonitis is absent.

Ocular Neuroses.—Here the observations are quite as numerous as those on the nervous disturbances of other organs. In the first place we meet with the painful sensations which correspond to neuralgia or, where the pain is continuous, more to a neuritis. When the eyes are at rest, and at night, the pains are relieved, but they are increased by pressure or when the ocular muscles are in motion, particularly in near work. Saemisch considers these neuralgic pains analogous to the so-called symptomatic neuralgias that we meet with in malaria, smallpox, and typhoid fever. Eversbusch assumes an affection of the muscles themselves, resembling the myositis in trichinosis. Gradenigo attempts a more definite explanation by implicating the sympathetic and the increase of intraocular pressure. Aside from the impediment to muscular activity, which is induced by the pain, there may be interference also with the motor functions, in which, without the symptoms of any nerve affection, the inner or outer muscular tissue of the eyes is involved. We are here dealing with a disturbance of accom-

modation, partly in the form of an accommodation asthenopia, but also with paretic symptoms. We will here mention the observations of Athoff, who observed an extreme bilateral paresis of accommodation in a case combined with ophthalmoplegia externa and paresis of the muscles of deglutition. Oppenheim attributed these symptoms to a polioencephalitis superior and inferior, also to a nuclear paralysis of the trochlear muscle and of the sphincter muscle of the pupil. However, we cannot altogether deny the possibility of a peripheral source, in which case the affection would present a greater similarity with those observed after diphtheria. In Athoff's other cases, there was a paresis of accommodation of varying intensity. These latter cases, according to Athoff, resemble more closely the picture of exophthalmoplegia externa, as it has been observed on a syphilitic, tabetic, or paralytic basis, or perhaps also after the ingestion of spoiled food. Fleischer and Koenigstein have described other forms of paralysis, as those of the rectus externus and trochlearis, which show a still greater similarity to postdiphtheritic paralyses.

The *retina* presents a comparatively small number of affections which can be referred to influenza. Saemisch has observed a few cases in which atrophy was present, but in which the characteristics of its neuritic origin were absent. He assumed the presence in this connection, on account of the extreme peripheral concentric contraction of the field of vision, of a retrobulbar process, mainly a lesion of the peripheral portions of the optic nerve, but left it open for discussion whether this lesion consists in a perineuritis or perhaps in a hemorrhage into the intervaginal spaces of the optic nerve accompanied by compression of the latter. The symptoms described here and there in literature refer either to retinal affections with a pathologico-anatomical basis, or to functional disturbances. To the former class Ehrlich refers the retinitis with exudation described by Dente, Rampsedie's case of detachment of the retina with hemorrhage of the retina, and a case observed in the clinic for diseases of the eyes at Bonn of embolism of the arteria centralis retinæ, not, however, involving the macular branch. Perhaps the case of Gutmann, presenting hyperæsthesia of the retina and marked hyperæmia of the optic nerve, and the case of Alt of partial loss of sight accompanied by ischæmia of the retina, also belong here.

The functional affections are confined to cases of amblyopia, in which an ophthalmoscopic examination did not reveal any anatomical cause, and to one observation of Sedan, who reported a sudden total loss of sight following an attack of influenza in a seven-year-old child. After twenty-four hours sight again returned and reached its former acuteness.

The *optic nerve* itself may become affected under the form of a retrobulbar optic neuritis, of an atrophy of the optic nerve, or of a papillitis. Atrophy of the optic nerve following influenza has been described by Bergmeister. Examination with the ophthalmoscope, after sight had markedly diminished, demonstrated an atrophy of the optic nerve accompanied by a dead-white appearance of the papilla, and contraction of the blood-vessels with cloudiness and thickening of their walls.

Braun describes affections of the optic nerve occurring in the course of neuritis multiplex. Vignes observed a marked papillitis in a woman who suddenly became totally blind on the eighth day of an attack of influenza. Among other peculiar disturbances there are some mentioned which are probably of central origin. In one case distinctly yellow vision was present, in other cases sparks and streaks of fire were seen. Eversbusch in his dissertation emphasizes the pain located deep within the eye; Parnet mentions cases of exophthalmic migraine; Holz observed a peculiar affection, which he looked upon as a paralysis of the right sympathetic.

Of the symptoms referable to the *circulatory system*, various cases of ecchymoses of the conjunctiva are to be mentioned, which should, however, perhaps be looked upon as frequently a result of the cough. Eversbusch demonstrated the presence of numerous small points and a dust-like cloudiness of the lens in a case during convalescence, the seat of which pointed to a change in the ciliary body, and he assumed this to be due to a hemorrhage in this portion, as no inflammatory exudative affection could be discovered. The case of embolism of the arteria centralis retinæ reported from the clinic for eye diseases at Bonn finds its place here too.

In no case have we been fortunate enough to prove satisfactorily the connection of the eye diseases with influenza by finding the bacilli of influenza. The occurrence of the graver diseases of the eye during influenza is in any case infrequent.

Affections of the Ear.

The extension of inflammatory processes from the pharynx and the nose to the organ of hearing may occur so readily that the frequency of complicating ear affections is thus easily explained. The attention of the profession in Germany has been especially drawn to the inflammatory affections of the ear by the bacteriological work of Kossel. In influenza, affections of the organ of hearing have undoubtedly been frequently overlooked, and it is to be assumed that many cases of cerebral irritation and pain in the head of various kinds have their origin in inflammation of the ear. On the other

hand, the ear affection has frequently made its appearance during the period of convalescence, when the patient had already passed from under the care of the physician. Aural specialists agree that ear affections are unusually frequent during an epidemic of influenza. Thus, Gruber observed during the months of November and December, 1887, and January, 1888, eighty-four cases of acute inflammation of the middle ear, but from November, 1889, to January, 1890, six hundred and twenty-five cases. Politzer also saw four times as many cases of middle-ear inflammation during the period of influenza as in the same months of previous years. The statistics in larger reports show that ear diseases are met with in varying proportions, from .05 to 2 per cent. of the total number of cases of influenza. The reports of Gruber in Vienna show that nearly twice as many cases of acute middle-ear affections were observed in his clinic during the epidemic as in the previous year. Many others also mention the increased number of cases of this complication. The first one in Germany to direct greater attention to diseases of the ear in influenza was Patrzek, who was followed by Neumann. Many of these cases of influenzal otitis are to be looked upon as secondary affections, this opinion being based on bacteriological findings, which we possess in great numbers, and which demonstrate the presence of staphylococci, diplococci, or streptococci in inflammations of this kind. Ribbert and Finkler found the streptococci to predominate in Bonn; Zafel and Weichselbaum met with streptococci and with diplococci; Lewy and Fraenkel found the diplococci to predominate in the pus of otitis. In 1892 Scheibe presented proof of the presence of Pfeiffer's influenza bacilli in the pus of otitis media. In many of these cases doubtless the infection is to be looked upon as a metastasis, while in others a direct extension by way of the Eustachian tubes is to be assumed. In the latter case the bacteria either find their way into the middle ear by gradual migration, or else they are propelled to this location by violent paroxysms of cough or forcible blowing of the nose. It goes without saying that inflammation of the middle ear may also take on the character of a mixed infection, or a number of bacteria which produce pus may give rise to the successive symptoms. The intercurrence of inflammatory affections of the ear, earache, and purulent otitis during the influenza epidemics of 1580 and 1729 has already been mentioned.

As regards the form of the ear affection, the greater number of observers have attempted to make a distinction between affections of the auditory apparatus, which are looked upon as a localized form of influenza, and such as are considered sequelæ to influenza. True influenzal otitis is said to be characterized by a peculiar condition of

the membrana tympani. The symptoms are those ascribed in the text-books to the affection known as myringitis hæmorrhagica bullosa, a condition previously regarded as occurring only in typhoid fever and variola.

The morbid condition of the tympanum in many instances gives rise to the most prominent symptoms. In this form of myringitis a sero-sanguinolent discharge takes place, and the affection is ushered in at an early stage of the influenza, soon after the beginning of the fever or shortly after its cessation, and is accompanied by violent symptoms on the part of the ear. All cases begin with great intensity as regards the subjective as well as the objective symptoms; dulness of the mind, headache, and pain in the affected ear are frequently complained of. The degree of deafness present is variously described. Occasionally we meet with total deafness, in other cases abnormal auditory sensations are complained of.

Among the objective symptoms the changes occurring in the tympanum are characteristic. The latter presents a deep bluish-red or blue-black color throughout its whole circumference; it is convex, mottled on its surface, or of a peculiar iridescent glimmer. In other cases, dark bluish-black hemorrhagic vesicles stand out on the red membrane, but there is no tumefaction of the papillary tubercle present. The disease runs a short course; in many cases the pain has already disappeared by the end of twenty-four hours. When the exudate is evacuated by paracentesis or spontaneous perforation of the drum membrane, it is said frequently to assume early a purulent character. Paracentesis is condemned absolutely by some. The point at which spontaneous perforation occurs in the tympanum, namely, the anterior lower quadrant, is also looked upon as characteristic of this form of otitis.

Of the other affections otitis media should be mentioned; it runs its course under the catarrhal or the purulent form. The otitis of influenza is distinguished from ordinary otitis media by the frequent involvement of the papillary tubercle. Gruber especially emphasizes the fact that the bony substance of the papillary tubercle very frequently becomes inflamed soon after the beginning of the disease, and that a periostitis in the vicinity of the papillary tubercle often occurs. In consequence of this, in many cases, an abscess forms in the bone and the soft parts of the papillary tubercle. A primary ostitis of the latter not involving the middle ear is also among the possibilities. These affections become dangerous mainly through extension of the inflammation to the meninges. But aside from this, death may be the direct result of the otitis media. In the greater number of cases, however, the prognosis is more favorable in influenzal

otitis than in that following scarlet fever, meningitis, or typhoid fever.

The occurrence of an otitis externa with the formation of hemorrhagic vesicles on the surface of the auditory canal should be mentioned; also the rare occurrence of labyrinthine disease, neuralgic otitis, auditory hyperæsthesias, and tinnitus aurium. Disturbances of hearing occurring during an attack of influenzal otitis are as a rule only temporary, but they have been known to last two or three weeks. In those cases in which the disturbances of hearing were permanent, an affection of the labyrinth was obviously present. I have observed a case of this kind marked by the sudden appearance of vertigo, tinnitus aurium, and deafness, in the absence of inflammatory symptoms, and without vomiting.

Mortality.

As regards the influence exerted by influenza on the general *mortality* rate, the data presented by Kruse recently in his work on the decrease of mortality during the last decade are very remarkable. He found that the mortality from tuberculosis, which is by far the most important cause of death, decreased most remarkably during the period of record in Prussia which extended over twenty years, from 1875 to 1895. The decline of mortality dated especially from the year 1886. On the other hand there was a marked increase in the death-rate from bronchitis and pneumonia in the years 1890 to 1894, which was obviously dependent on the influenza epidemic.

According to the official records there died of influenza in Prussia, in 1890, 9,576 persons; in 1891, 8,050; in 1892, 15,911; in 1893, 10,403; and in 1894, 7,336. Of these more than one-half were over sixty years of age.

Prophylaxis.

According to modern views, prophylaxis occupies the first position in our therapeutic endeavors, and its conception must also be so widely extended that not only should we attempt to fortify the individual against the influenza bacillus, but we should also endeavor to protect the patient against any further advance of the bacilli and consequent secondary infection. And here we are primarily met with the question whether we are able to secure immunity against influenza. This unfortunately does not seem to be the case.

The existence of a congenital immunity against influenza in certain individuals seems problematical, for the examples cited to prove this, where one or another person, surrounded by influenza patients,

has escaped the disease, are not sufficient ground for the belief that there is a true immunity. I myself came into very close contact with influenza patients during the great pandemic, remaining altogether free from the disease, and yet suffered from an extraordinarily severe attack of the infection at the close of the epidemic in the year 1891. It seems to me to be largely a matter of chance whether one escapes or not during an epidemic of influenza. Immunization experiments made on animals have proved unsuccessful, and it may be said that we have not yet succeeded in preparing an anti-influenzal serum for prophylactic and therapeutic purposes.

The question then arises whether we cannot protect persons against influenza by isolating them. To do this is certainly beset with extraordinary difficulties. During a pandemic visitation the individual would have to retire to the greatest solitude to escape the disease, and this, in the case of most people in active life, seems almost an impossibility. There is no question, however, that a person may be prevented from catching the disease by means of strict isolation. Accordingly the indication is undoubtedly to place patients suffering from lung affections, or delicate persons whose life may be threatened by an attack of influenza, so far as circumstances will permit, beyond the reach of the infection. My own observations have taught me that phthisical patients especially may for a long period carry the influenza bacilli about with them, and I would most energetically insist that everything imaginable should be done in sanatoria, or where many tuberculous patients are congregated, to avoid infection. Upon the reception of new patients in these places, an examination of the bronchial secretions for influenza bacilli should be made, for the reason that it is especially in the tuberculous that influenza is liable to cause death. There is no doubt whatever that special danger of contracting influenza exists at the various spas and climatic health resorts to which convalescents flock. It would therefore be wise for every patient suffering from bronchitis, even though not tuberculous, or from any pulmonary disease, to observe the greatest care while in these resorts to prevent infection by influenza. Under these circumstances, isolation is of a far-reaching importance. We are not to think that in face of the extraordinarily contagious nature of influenza all attempts at prophylaxis are necessarily useless, but, recognizing this fact, should rather redouble our efforts in the way of prevention. In the first place the destruction of the influenza material is to be considered, in addition to the isolation of the patient, and therefore we should demand under all circumstances that the sputum be deposited in vessels supplied for this purpose, and that it be most carefully disinfected. The disinfection of the linen

and of all articles in general use should be most strictly insisted on in hospitals and sanatoria. Cholera was not thought to be controllable formerly, and yet in recent years we have succeeded, in spite of the appearance of this disease in many distinct localities, to prevent its occurrence in a widespread epidemic form.

It will prove to be much more difficult to attain prophylaxis by medical measures, yet the attempt should certainly be made in this direction. As the invasion of influenza bacilli so frequently takes place by way of the mouth and nose, the irrigation of these cavities with disinfecting solutions seems justified. Gargles, nasal sprays, and inhalations of various kinds are recommended for this purpose, the favorite drugs being creolin, menthol, quinine, oil of eucalyptus, camphor, oil of peppermint, and other ethereal oils.

The internal use of medicaments, especially of quinine, has been resorted to, experience having taught us that the latter could be administered with good results as a prophylactic agent against malaria. We have knowledge of the experimental use of quinine in this manner by Graeser. Graeser's observations include the cases of influenza treated at the Polyklinik of Bonn, and experimental treatment of a regiment of hussars stationed at that place. The results obtained in these cases were as follows: In Bonn all the men of one squadron were given 0.5 gm. (gr. viiss.) of quinine in 15 gm. (℥ ss.) of whiskey for a period of twenty-two days. During this experiment there became ill in the first squadron, 22 men; in the second, 7; in the third, 19; in the fourth, 42; and in the fifth, 32. The second squadron was that in which the quinine and whiskey had been given to the men. Out of the seven cases of sickness occurring in this squadron, three may fairly be excluded, because the disease made its appearance after the termination of the experimental period. The four remaining cases occurred on the second, fourth, fifth, and sixth day respectively of experimentation; after this period no more cases of influenza occurred in the second squadron while the quinine was being given, although the disease continued to progress in the others. This result cannot be due to chance.

Treatment.

Among the drugs employed with a curative object also, quinine occupies a front rank. Observations made on the patients in the Polyklinik at Bonn demonstrated that out of the eighty persons treated with quinine only three made their appearance at the Polyklinik the second time, while of those treated with other drugs, nearly one-half reappeared twice or more frequently. From this we are jus-

tified in believing that quinine exerted a favorable influence, and this opinion need not be shaken by the impressions received in other places that quinine exerted no influence on the course of the disease. The favorable action of this drug has besides been observed by Dujardin-Beaumetz, Teissier, Carrière, Přibram, and others. Mossé, of Paris, also ascribes to quinine a prophylactic and abortive action in influenza. To abort the disease, he administered 1 to 1.25 gm. (gr. xv.–xx.) on the first day, and at times also on the second day. Filatow, in Moscow, has also observed the favorable action of quinine, especially in children. Others, as Eichhorst, Tranjen, and Bowie, had no success in the use of the remedy, while Leichtenstern believed that the cases treated with large doses of quinine as a rule did worse than those which were not so treated. In the German collective investigation reports we find that some physicians praised quinine as giving them brilliant results, while others were greatly disappointed in its effects. This divergence is hard to explain, because we know nothing of the histories of the different cases or of the manner in which the quinine was exhibited. It would be wrong, however, to thrust aside the positive statements of trustworthy observers.

Of other remedies to which have been attributed a special action on the disease may be mentioned antipyrin, antifebrin, phenacetin, salipyrin, and salicylate of sodium. Each one of these remedies has had its special advocates. That their action is an antineuralgic one is conceded, but we cannot doubt that antipyrin especially, and also salipyrin, produce wonderfully favorable results in influenza. The beneficial action of these remedies consists not only in the lowering of temperature, but also in a favorable influence on all the nervous symptoms. Pain is quieted, that of the nerves themselves, as well as that of the joints, the bones, and the muscles. The subjective condition is improved, and there are cases on record in which extraordinarily striking effects of these drugs on some of the grave symptoms were observed. In affections of the eye and ear these remedies have also been effectual. A case in which a marked hyperidrosis was at once cured by salipyrin has been previously reported by me, and we therefore cannot deny the specific action of antipyrin and salipyrin on the toxic conditions. Antifebrin is much less serviceable than antipyrin, phenacetin, and salipyrin, but salophen and migranin have been tried with good results.

Drewes, in Hamburg, especially lauds the action of salophen and ranks it above salicylic acid and salicylate of sodium. In violent attacks of nervous influenza he employed salophen in doses of 2 gm. (gr. xxx.) increased to 5 or 6 gm. (℥i.–iss.) a day. In the case of children he gave 0.3 to 0.5 gm. (gr. v.–viiss.). I believe that most

physicians have arrived at the point where they would not like to do without these preparations in influenza, but it should certainly not be forgotten that reports of this kind have quite frequently been used for advertising purposes.

Oil of eucalyptus was also for a time regarded by the English as a panacea for influenza, and cuspidors, the floors of rooms, etc., were frequently flooded with eucalyptus. I have met a man who even rubbed oil of eucalyptus into his hair, to protect himself against influenza. Such ridiculous actions are naturally the result of ingenious advertisements preying upon the fear of the general public.

Iodine and mercury have been much in use and more or less strongly commended.

Digitalis has also frequently been found useful in influenza. Huchard, of Paris, recommends more especially digitalin, administering it in a 1:1,000 solution, thirty, forty, or fifty drops to be taken during the day; at the same time he puts his patients on a strict milk diet. Should the indication for digitalis reappear during the course of the disease, he orders the solution to be taken in smaller doses, twenty to thirty drops. In cases of gastric influenza he recommends salicylate of bismuth, naphthol, and salol, but, above all, benzonaphthol, five to six pills daily, each one containing 5 mgm. (gr. $\frac{1}{12}$).

Benzol is recommended by Robertson in doses of three drops for children or five drops for adults, every two or three hours. This medication should be continued for three or four days after all symptoms of the disease have disappeared.

Simson in London reports especially favorable results from carbolic acid, which was employed by him in many hundred cases, in children as well as in the aged. The dose is two drops three times a day.

As we cannot with certainty rely on the specific action of any one remedy, symptomatic treatment is often imperative. In disease of the bronchi, expectorants and emetics are frequently of great benefit. In this connection, however, I wish to sound a note of warning as to the employment of apomorphine, for the reason that the latter is liable frequently to cause cardiac failure; on the other hand, I would recommend the exhibition of ipecacuanha and Dover's powder. In combination with quinine or disinfecting substances, such as guaiacol and terpin hydrate, this mixture has an excellent effect on the bronchial secretion and the cough.

Among the disinfecting drugs camphor should especially be mentioned, as it is at the same time indicated in heart failure; we should especially keep in mind the subcutaneous administration of cam-

phorated oil. Alcohol has been frequently employed as a heart stimulant, and has also been recommended as a prophylactic. Strong alcoholic liquors, however, usually increase the headache, although their value in heart failure is undoubted.

Hydrotherapy is not generally recognized as effective. The use of Turkish baths in all stages of the disease is not to be recommended in every case. Various symptoms, as for example a high temperature and headache, are unfavorably influenced by them, and the bringing on of perspiration in patients sick with influenza is as a rule not indicated. On the other hand, careful sponging with tepid or cool water and moist packs have in many cases been beneficial. Pneumonia especially is favorably influenced by the wet pack, and more especially are the subjective symptoms accompanying it, for example dyspnœa, rendered less severe. Treatment by means of cold baths has not given favorable results.

In reviewing all these methods of treatment we come to the conclusion that many of them belonged to the experimental period, and it does not appear superfluous to add some remarks on the manner in which such experiments should be conducted. If a careful medical control is necessary in any acute infectious disease as regards the action of different remedies or the methods employed, it is doubly so in the turbulent course of influenza. The senseless employment of antipyrin, as well as of other measures for reducing the temperature, must undoubtedly have been harmful in many cases, and it cannot be too strongly urged that in the treatment of influenza all routine measures should on principle be avoided. Especial care should be given, during convalescence, to the improvement of the general strength, for the reason that a great number of sequelæ of an inflammatory and nervous nature, including psychoses, may be referred back to debilitated conditions resulting from an attack of influenza.

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TYPHUS FEVER.

BY

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TYPHUS FEVER.

Synonyms.—Spotted fever, Jail, Camp, or Ship fever, etc.; Span., *Tifo, Tabardillo;* Ger., *Fleckfieber;* Fr., *Fièvre pétéchiale.*

History.

It is very necessary to study, though briefly, the history of typhus fever, as a knowledge of it will be of service in supplying us with certain facts relative to the etiology of the disease.

We do not know the exact period at which typhus fever appeared for the first time, although we find no description of it in any writings prior to the beginning of the sixteenth century. We find, indeed, that typhus fever occurred in epidemic form in Italy from 1505 to 1508, and again from 1524 to 1530. Fracastor, a physician of Verona, was the historian of the epidemic. From Italy the disease spread to France, Spain, Hungary, Austria, Bohemia, Germany, and Sweden in the course of the sixteenth century, returning to Italy at the end of this century.

The epidemics of the seventeenth century, in which typhus fever was accompanied by dysentery and scurvy, were the consequences of the wars and famine which ravaged all Europe in this memorable epoch.

In the eighteenth century typhus fever existed in endemic form in almost every country of the Old World, assuming an epidemic character in various regions whenever want and misery made themselves especially felt. The French Revolution, in the closing years of that century, carried war to all parts; and in the first fifteen years of the nineteenth century, the Republic first and later the Empire sent everywhere the French armies carrying with them war, famine, and typhus fever. This last travelled with the conquerors or remained with the conquered, and in both ways settled down upon the larger towns, which thus became foci for the origin and spread of epidemics.

Since 1815 there have been no epidemics embracing the entire continent of Europe, but the disease has remained in endemic form in many countries. Ireland has been a permanent centre of the disease, which has assumed an epidemic character in that country five

times within the present century. In Russia typhus fever has been endemic in many parts, especially in Poland, and has also had epidemic exacerbations at various times, especially from 1854 to 1856, during the Crimean war. In consequence of a similar calamity, the Russo-Turkish war in 1877–78, a great epidemic occurred in Russia, attacking one hundred thousand men and killing fifty thousand.

Several historians of the peoples which inhabited el Anáhuac (the central plateau of Mexico) in ancient times have given a description of a disease which was known to the natives before the conquest by the name of "cocolistle." But the oldest and most authentic notice which we have of an epidemic of fever marked by a spotted eruption on the skin is that which raged in Mexico in the year 1530. This epidemic caused great ravages, and it is noteworthy that it coincided with the epidemic of typhus fever which was raging at the same time in Spain. In 1545 there was another epidemic in New Spain, the characters of which have not been well described by historians, but which might with great probability be regarded as typhus fever by reason of the short interval which separated it from the former epidemic, and also because of the great mortality, which reached eight hundred thousand. Making all allowances for exaggeration in this figure, the mortality was undoubtedly very high and comparable with that from typhus fever at the same period in Europe. In the years 1575–77 there spread throughout New Spain great epidemics of a disease known by the name of "matlazáhuatl," which, from the description given by Dr. Juan de la Fuente of the disease as he observed it in his patients, was most probably typhus fever. The natives were special sufferers from these epidemics, great numbers of them perishing. There were other epidemics in the years from 1624 to 1714, of which we possess no accounts.

In 1736–37 there was another epidemic of "matlazáhuatl," which presented many of the characters of typhus fever but which was accompanied by a yellow coloration of the skin, from which fact some have been led to believe that the disease was yellow fever. But we cannot accept this view, since this last-named disease never prevails in the central tableland of Mexico. This epidemic was attended by a heavy mortality which the historians of that period place as high as one hundred and ninety-two thousand. The epidemic recurred in 1763; the disease was exceedingly contagious, as on the previous occasion, and was marked by nasal hemorrhages. In the years 1805, 1812, and 1813 there were epidemics in the valley of Mexico, which were probably of typhus fever and which also caused many deaths.

In the republic of Mexico the disease prevails in endemic form in the central plateau, but has only very rarely extended over limited

areas on the Gulf and Pacific coasts of the country. While the disease is endemic in the chief cities and towns in the elevated regions, it presents almost constantly exacerbations during the winter, and these not rarely assume an epidemic form. The most notable of these epidemics occurred in the years 1821, 1835–38, 1848–49, and the most important of all in 1861. This epidemic was spread by the armies which overran the country during the war of the Reforma. The last epidemic was that of 1892–93, following several successive years of scarcity and failure of crops. During the period from 1861 to 1893 there were numerous partial epidemics in the Mexican federal district and in various states of the republic.

In the United States and Canada the Irish immigrants often brought in the disease. Its ravages were most marked among the immigrants themselves, but it also extended to the other inhabitants of the larger cities of the East, such as New York, Boston, Philadelphia, Baltimore, etc.

Etiology.

The infectious nature of typhus fever, the manifest resemblance which it bears to other infectious diseases, and its confusion with some of the latter, even in quite recent times, render it very probable that the disease is due to a microorganism. We shall first consider the well-established facts in the etiology of typhus fever and later discuss those which appear to us to be still doubtful.

Typhus fever is contagious; the facts which go to establish this proposition are numerous, but we shall take up only a few of them. If the disease attacks one member of a poor family dwelling in a small apartment or a single room, where the patient is in close contact with the rest of the family, we very commonly find a certain number of the latter contracting the disease. In these cases contagion is favored not only by direct contact of the sick and the well, but also by the bad conditions under which the people live; neither the patient nor those about him ever change their body linen or their bedclothes, if they have any. In the epidemic which prevailed in France in 1893 facts of this sort were noted, especially in the Island of Tudy, in which a single family furnished fifty per cent. of all the cases. Night shelters, in which the occupants sleep closely crowded together, and hotels and lodging-houses of the lowest grade, in which similar conditions prevail, furnish the greatest number of cases of contagion.

In contrast with this we may say that contagion is seldom in evidence when the disease appears among those in easy circumstances,

in a house in which the patient may be isolated in a room from which have been removed all carpets, rugs, and tapestries, and in which there is left only the indispensable furniture; when the linen of the patient is changed daily; when special attention is paid to maintaining cleanliness of the mouth, nose, and intestinal tract; and when the attendants wash their hands frequently, especially before eating. Under these conditions we may say that typhus fever is not contagious.

In hospitals, however, and during an epidemic period, contagion is the rule, and it is the more certain the longer is the time during which the attendants remain in the company of the sick. Stokes and Cusak say that in the epidemics in Ireland from 1813 to 1848 there were among physicians 568 cases of typhus fever with 132 deaths, approximately 46 per cent. of all cases and 10.5 per cent. of deaths. In the Crimean war (1854–56), during the height of the epidemic, in a single period of fifty-seven days typhus fever attacked 603 nurses in a total of 840 in the service, and caused the death of 80 army surgeons. In the Russo-Turkish war 60 per cent. of the physicians, 80 per cent. of the orderlies, and all of the Sisters of Charity were attacked. In Similizi, Sistova, and Rasgrad the hospital *personnel* had to be renewed three times because of the ravages of typhus fever.

In the great epidemic through which we passed in Mexico in 1860–62 a large number of physicians in civil life and very many army surgeons died of typhus fever. During the typhus epidemic in Mexico in 1876 Dr. Orvañanos observed the following fact: "In the Hospital de Jesús in Mexico City there fell ill a son of the superintendent (*maestro de obras*); on the floor above him slept the seamstress of the hospital, who acquired the affection in a short while. She was placed in bed 7 in the female ward; soon afterwards the patients in beds 6 and 8 took the disease, and these in their turn communicated it to five other patients in the immediately adjacent beds, but the fever was not contracted by any occupants of the beds on the opposite side of the ward, distant from the preceding about four yards. The ward was emptied of its occupants, only those with typhus fever being left, and the epidemic ceased."

Another curious fact is the following: "A convalescent from typhus fever in the Hospital Juárez in Mexico City, in which patients with this disease are treated, began to present symptoms of mental disorder and was transferred to the Hospital de San Hipólito in the same city. In this hospital an epidemic of typhus then broke out in the department to which this convalescent was assigned; all those attacked were at once sent to the Hospital Juárez for treatment, and the epidemic ceased suddenly, but broke out again in a few days

when the convalescents began to be sent back from the Hospital Juárez. Since all the drains and closets had been cleaned and the wards in which typhus had occurred had been disinfected, under the direction of the Superior Council of Health, it is very evident that the cause of the new invasion was the clothing worn by the patients, which was the same that they had had on when they were sent to the Hospital Juárez. The Superior Council of Health ordered that the convalescents, on returning to the Hospital de San Hipólito, should take a bath and that their clothing should be disinfected. These measures were completely successful, and no other case of typhus fever occurred in San Hipólito."

When typhus fever breaks out in armies during a campaign the troops spread it abroad, carrying it to the various towns through which they march, as we saw in the section on the history of the disease. In Mexico, during the war of the Reforma, the liberal army spread typhus fever throughout the Mesa Central del Anáhuac, or Central Plateau. The disease attacked a large number of the surgeons who had the care of the sick soldiers, and the greater part of them perished.

The following fact in support of the theory of contagion I find recorded by Netter[1]: Mrs. J. travelled in a coach with her two sons and a man named N. In the latter part of January they gave shelter to a tramp whom they found dying on the highway. They left this patient the following day and resumed their journey. On the 8th or 10th of February they felt ill and consulted a physician, who advised them to go to a hospital. The two boys entered the hospital on February 19th, but the woman J. and her lover N. went to another town and slept in the house of the mother of J., who was the wife of M. This woman, her son, and the three children of J., who lived with their grandmother, all fell sick and were taken to the hospital on March 11th. The sister and sister-in-law of J., who had taken care of M.'s family, and the physician who had treated them contracted typhus fever. N., the lover of J., went to his own home and after his arrival five members of the family were taken ill with typhus. Finally a Sister of Charity, who nursed them, also fell sick.

I am indebted to Dr. Ruiz Erdozáin for the history of the following recent case, in which the effect of contagion was very apparent: In a house in the city of Mexico in which seven healthy persons lived was received as a guest for one night only a person who felt ill that same night but who left the house the following day. He continued to be ill, and it was found that he was suffering from typhus fever. Three days later the lady of the house fell ill of typhus, and the remaining six persons took the disease one after the other. Of

the eight persons four died, among them the guest who had introduced the disease into the household.

These facts demonstrate that typhus fever is transmitted from the sick to the well by direct contact, but that the contagious principle may also be carried by inanimate objects which have been in contact with the patient; for example, a healthy person who sleeps on a bed previously occupied by a typhus-fever patient will very probably contract the disease. Clothing may convey the disease, as is shown by the epidemic in the Hospital de San Hipólito, described above, and by the following case which I have observed. A sister of Mr. C., a person well known in Mexican society, fell ill with typhus fever. The clothing of the patient was changed two or three times a day, and her own supply becoming exhausted some belonging to her sister was taken for her use. The lady died, and her sisters had the clothing belonging to them, which the patient had worn, washed and ironed; disinfection was not made use of at the period at which this incident occurred. The clothing was not worn, however, until eight months had elapsed, but within a few days after they had put on these garments the two sisters were taken ill with typhus fever. This case shows not only that the disease may be transmitted by clothing but also that the germ of typhus fever may retain its activity for at least eight months.

Dr. Orvañanos had observed a case in which typhus fever was carried from the sick to a well person living in a house at quite a distance from the former, the linen of the second person being washed together with that of the one who was first taken ill. Similar facts are to be found in the literature of typhus fever.

The chances of acquiring the disease by contagion are very great when a healthy but susceptible person enters a room where many typhus-fever patients are lying, or a ward of a typhus-fever hospital, or a closed or badly ventilated room in which a patient with typhus is lying; or when the person exposed is convalescent or actually suffering from some other debilitating disease, such as scurvy or dysentery. While I know of cases in which a single visit to a typhus-fever patient has sufficed to give the disease, yet the experience of physicians in all countries shows us that the danger of contagion is greater in proportion to the frequency and duration of the contact with the sick. It has been observed in hospitals that the nurses and sisters who are brought most intimately and most frequently in relation with the patients furnish the greatest number of cases of the disease; that after them come the physicians and the students who make the visits with them; and that in the third rank come the medical inspectors and other officials of the health department. The

danger of contagion is greatest when many patients are congregated in one place, when ventilation is insufficient or absent, and when the linen and bedclothing of the patient are not changed.

As negative proof I may repeat what I said above, a fact well known to all physicians in Mexico, that in the case of a typhus-fever patient of the upper classes, occupying a room by himself which is thoroughly ventilated day and night, whose clothes are changed once or twice a day, and whose dejections are removed at once and carefully disinfected, the disease does not attack the attendants.

Since objection might be raised in regard to the cases above related that the disease could have been acquired by other means than infection, we may refer to the statistics collected by French physicians in the Crimean war, according to which it is seen that in the general wards 13 physicians and 3 sisters remained free from the disease and that among 125 patients 1 only contracted the affection; on the other hand, in the wards where typhus-fever patients were received, of the 6 sisters 3 were attacked, of the 14 physicians 4, and of the 127 nurses and orderlies 57. This demonstrates that the disease was spread by contagion.

The data of this same war show that the English and French were encamped in the same place and that they were subjected to the same discipline and suffered the same fatigues, yet typhus fever prevailed much more extensively among the French than among the English. The explanation of this difference was that the tents of the English were pitched far apart, that their barracks were spacious and well ventilated, and that their food was better.

Another important fact is that in hospitals in which the patients are much crowded and in which the ventilation is bad, typhus fever assumes a more grave form, as was seen after the battle of Leipsic. Those who were treated in the hospitals of Mayence and Cologne, in which they were literally herded together, suffered a much greater mortality than those who were attended in the open courts because there was no room for them in the wards. I was witness of a similar fact in 1861, when I was beginning my medical studies. At that time private patients were treated in closed rooms, in which there was but little circulation of air, and the mortality among them was much greater than among hospital patients who were treated in large wards the windows of which were kept open the entire day.

Contagion may also occur by means of various objects which the sick have used, as is evidenced by the following case narrated by Pringle, and which is repeated in all treatises on typhus fever. When the English army was waging war in Germany in 1743 there were received at Gand a large number of tents in which typhus-fever

patients had been treated. These tents were given for repair to a workman in the city, and he and twenty-three others who had assisted him in the work were taken down with typhus fever and seventeen of them died. Typhus fever was not present at that time in Gand, and none of the workmen who were engaged in repairing the tents had had any communication with the typhus-fever patients among the soldiers.

The place occupied by a typhus-fever patient in the ward of a hospital may retain the contagion and pass it on to this patient's successor. It has been noted in the Health Department of Mexico, under which an inspection is made of houses where typhus fever has occurred, that the disease often attacks in succession all who occupy the infected dwelling unless a thorough disinfection of the premises has been made. The contagious principle may be preserved in the walls of rooms in which typhus-fever patients have been cared for, as the following case, for an account of which I am indebted to Dr. Ponce, of Telancingo, demonstrates. During the course of the epidemic which prevailed in that city in 1890, a wooden hut was used for the isolation of the sick. At the end of the epidemic this hut was abandoned, and remained empty until February, 1896, when an order was given to destroy it. Nine persons were present during the demolition of the building, some of whom actually were engaged in the work while others were on-lookers simply; all of these were taken ill with typhus fever, seven died and two recovered. At this time there were no cases of typhus fever in Telancingo. This fact proves not only that the germ of typhus fever may remain in the walls of a house but also that it may preserve its infectiousness for six years.

So long as the microorganism of typhus fever remains undiscovered, and as the organ or organs in which it resides and the manner in which it makes its exit from the body are unknown, we are not able to determine positively the mechanism of contagion. Although the data having reference to the etiology of typhus fever are as yet rather vague, I think it will be well to review them, since they have a bearing upon the prophylaxis of the disease.

For a long while the skin, more especially the scales given off from the characteristic eruption of the disease, has been supposed to contain the contagious principle, this belief being based upon the facts above related that the patient's underclothing, his bedclothing, the mattress upon which he lay, and the tent which sheltered him have served as means of conveying the disease.

It has been supposed also that the microbes may be scattered by means of the sputum, dried and carried about in the atmosphere, this belief finding its support in the following observation of Chantemesse.

In Lille an advocate, a commissary, and an attendant in the court were attacked with typhus fever although they had had no communication with any one suffering from the disease. Investigation showed that these persons could not have acquired the contagion elsewhere than in the police court, where every day were brought together a great many tramps and other men coming from the most infected quarters of the city, who always left behind them a large quantity of expectorated matter on the floor. This matter became dry and was thrown into the air on the following day, when the court-room was swept without any precaution being taken to sprinkle the floor. As may be seen, however, this fact is not conclusive.

We may regard the fecal discharges, and in general all the excretions, as probably of greater importance in an etiological sense. Among physicians practising in Mexico the belief is very prevalent that typhus fever may be contracted by inhaling the emanations from water-closets, drains, or obstructed sewers. Infection through fecal matter in process of decomposition is the only cause to which could be attributed many small epidemics, especially one which occurred some years ago in the Hospicio de Pobres in the city of Mexico. Dr. Nicolás Ramírez de Arellano, member of the Superior Council of Health, described this very interesting case, as regards the question of infection, at the meeting of the American Public Health Association in 1892. In 1892 the house drains became clogged in front of the children's dormitory in the Hospicio de Pobres. Very imprudently the drains were opened, and the fecal contents were removed and placed in front of this same dormitory. The children sleeping there were attacked with typhus fever, and the epidemic continued until the obstruction was removed and the drains were disinfected and closed; then only it disappeared completely.

The same author has reported the following: "The epidemic which occurred in the School of Correction in September, 1882, was undoubtedly due to the same cause. It began among the inmates of the asylum, who occupied a dormitory situated at the northern end of the first courtyard of the building, the back windows of which looked out upon the second courtyard, where at that time were located the privies of the institution. These were kept in such bad condition that the contents overflowed a portion of the yard. As I said this dormitory was the first invaded, and for more than twenty days all the inmates who were attacked with typhus fever were of those who slept in it, and only at the expiration of that time the children occupying other dormitories began to be attacked, the total number of cases being about one hundred. It is to be noted that at the entrance to the dormitory in which the first cases occurred there was a closet

unprovided with traps, which communicated with the general sewer; and notwithstanding the cleanliness which was here maintained the atmosphere of the dormitory, in which the ventilation was not good, was loaded with bad odors. The sick were isolated, disinfection was made, the rooms were well ventilated, the water-closet in the dormitory was removed, and the others were repaired, the leaks being stopped; in this way the disappearance of the epidemic was effected, and no cases have occurred in the institution since."

The writer just quoted adds: "Innumerable are the houses in which an inspection made on account of an outbreak of typhus fever shows sewers without any flow, stopped up with fecal matter in process of decomposition. I have records of many very curious observations concerning infected houses in which the epidemic ceased the moment the closets and sewers were cleansed."

According to the reports of the sanitary inspectors of the city of Mexico, typhus fever could be attributed to the emanations from fecal matters in process of decomposition in 1,108 cases out of a total of 5,749 inspections.[2]

The soil of Mexico city, which is made ground in some streets, is formed of detritus from demolished buildings and refuse of all kinds, and the subsoil immediately beneath is saturated with liquids soaking through the walls of vaults and sewers loaded with organic matters in process of decomposition. Excavations which are made in the soil for the placing of water mains or gas pipes uncover this infected layer. Many of those who contract typhus fever, according to the testimony of responsible physicians, can point to no other cause for their disease than the emanations from these excavations.

The emanations alone from fecal matters in process of decomposition have sufficed satisfactorily to explain the occurrence of typhus fever in villages and on estates where there is no large collection of people; among those who have not been exposed to privations of any sort; and in communities in which there has been no antecedent case of typhus fever to which the infection might be attributed. Some of these villages and estates were situated in the plains of Apam which occupy elevated points in the central plateau of the country, swept by the winds which blow there incessantly.

As we have said before, bacteriology alone can solve these problems, but we have just spoken of emanations from fecal matters and this leads us to study the question whether or not the air may be a medium for the conduction of the germ of typhus fever. When an epidemic of typhus fever has broken out in the ward of a hospital it has been noted that the disease has travelled from bed to bed, and this has been attributed, and justly, to the fact that the air passing over

the patient took up the germs of the disease and transmitted them to his immediate neighbor. In these cases we cannot attribute the spread of the disease to contagion carried by the nurses, for were such the case the fever would be distributed generally throughout the ward and would not travel from bed to bed in regular order.

The fact, which I have previously mentioned, that individuals have contracted typhus fever at a time when it did not prevail epidemically, after having breathed in the effluvia from a water-closet, a drain, a sewer, or a recently opened excavation in infected soil, can be readily explained by admitting that the air may transport the germs from the infected place to the organs of the one who contracts the disease. But this transmission does not take place over long distances, as was formerly believed and as many believe at the present day. As we have already said, it is sufficient to place the patient in a room by himself and to shut off direct communication from the outside with his attendants, in order to prevent the spread of the disease. No case has ever been known of a typhus-fever patient in a house on one side of a street communicating his disease to persons living on the other side of the street, even when the width of the latter was no more than twelve or fifteen yards and when the windows of the two houses were constantly open. Some accurate observations of Brouardel[3] also confirm this view.

In the Hospital Juárez are received all those suffering from typhus fever who cannot be taken care of in their homes, either by reason of the impossibility of isolation or because they are unable to secure proper medical attendance. Yet there is no case on record in which the disease has been communicated to persons living in any of the houses in the streets surrounding the hospital. These facts show clearly that, although the air may be the agent of transmission of the contagion of typhus fever, it can be so only for short distances.

From what has been said it is seen that typhus fever may be transmitted from one ill with the disease to a healthy individual; but many medical authorities also hold that it may appear spontaneously in persons affected with various diseases. This mode of origin of typhus fever is known as the autochthonous.

According to the teaching of Hildebrand, autochthonous typhus may arise from other diseases; from the crowding together of many people; from the breathing in of animal emanations; from want; from exhaustion through overwork; from all those causes, in a word, which depress the vital powers. This doctrine has had many strong upholders, such as Murchison,[4] Fauvel, Jaccoud, Kelsch, and others. I cannot, in a work of this kind, recite all the detailed cases which are repeatedly quoted by the authors mentioned in support of this

assertion. These are cases of the appearance of typhus fever in certain districts following the failure of the crops for several successive years; of the appearance of the disease among those sentenced to the galleys and isolated strictly without the possibility of communicating with any typhus-fever patients; of the occurrence of typhus fever on shipboard among the French troops returning from the Crimea; or of the origin of the disease in overcrowded prisons. In all these cases the authors who report them assert that it was impossible to discover any cases of typhus fever, from which contagion might have come, among the communities or aggregations of soldiers or prisoners in which the epidemics occurred; and being unable to find any other explanation of the outbreak, the writers have been forced to take refuge in the belief in the spontaneous evolution of the malady.

In the great wars which devastated Europe in former ages and in the early years of this century there were united all these conditions which have been enumerated: hunger, fatigue, moral depression, privations of all sorts, crowding together of soldiers in ships serving as transports, and the distress resulting from prolonged sieges of fortified towns. A French physician, Kelsch,[1] expressing the opinions of all the military surgeons who witnessed the epidemic of typhus fever occurring in Algeria in 1866–68, has sustained with much talent and by the weight of very many facts the doctrine of the autochthonous origin of this disease. This writer believes that the starving bands of Arabs, who were in the last extremity of misery, suffering from diarrhœa and other diseases which had reduced them greatly, covered with rags, and filthy beyond expression, who came to the towns occupied by the French to beg food and shelter, gave rise to typhus fever among the French troops without themselves having the disease, although they had originated it.

Those who oppose this theory are very numerous. They explain the facts of the kind above narrated by affirming that the investigation has not been carried so far as to exclude the possibility of there having been a primary case of typhus fever to which the subsequent cases could be attributed. The partisans of the theory of direct or immediate contagion of typhus fever believe that want, crowding, overwork, and mental distress lower the resisting powers, predisposing the individual to the disease, and so convert the sporadic occurrence of typhus fever into an epidemic; but they insist upon the absolute necessity of the introduction of the disease into a place before other cases may develop there.

I ought to note that Kelsch, when he employs the word "autochthonous," does not mean spontaneous generation of the germ, but that this, which is commonly present in certain organs of the body,

acquires a renewed activity when it meets with conditions favorable to its development, such as are those above enumerated. He supports his theory with the authority of Pasteur, from whom he quotes the following paragraph: "There are other virulent diseases which appear spontaneously in one country or another, such as, for example, typhus fever in camps. Without any doubt the spores of the microbes which give rise to these diseases are scattered everywhere. Man carries them in himself, perhaps in the intestinal canal, without much injury, but they may at any time become dangerous, when their virulence becomes progressively increased under conditions of overcrowding, of successive reproduction on the surface of a wound, or in some other manner."

The opponents of the autochthonous theory of typhus fever, whose spokesman is Netter, say that when diseases are caused by germs which exist normally in the natural cavities of the body, these germs are frequently found there, as we see, for example, in the case of pneumonia, erysipelas, etc., but that this is not the case with typhus fever, which made its appearance recently in Paris after an absence of eighty years.

In order to account for the appearance of epidemic typhus fever in prisons where it had not previously existed, in ships after long voyages, or in other places where it had not before been observed, it has been necessary to resort to one of two explanations, namely, either a diminution of resistance of the individuals who are attacked or an increase in the virulence of the pathogenic germ. It is evident that all the causes above mentioned act by lowering the power of resistance of the individual; or to speak with greater precision in the language of science, they prepare a favorable soil for the growth of the typhus germ. As, however, it sometimes happens that there are no bad conditions existing in the individual, that is to say, the soil has not been rendered more favorable to the growth of the germ, we then have to invoke the factor of augmented virulence of the germ. And in fact, in localities where typhus fever is endemic, as throughout the central plateau of the Mexican republic, this disease assumes an epidemic prevalence in the winter season when rain seldom falls. This increase occurs almost simultaneously in Toluca, Querétaro, Guanajuato, Zacatecas, San Luis Potosí, Pachuca, and other cities of the central plateau. Graves[6] makes a similar observation as regards Ireland, and the same has been remarked by writers in other countries in which typhus fever is endemic.

My own opinion is that we have no right to sacrifice observed and attested facts to the lack of a satisfactory explanation of their causes; and that we ought to cherish the hope that our science, as it pro-

gresses, will give us the key, which at present is not in our possession, that will enable us to discover the primary cause of typhus fever; and we must content ourselves in the mean while with noting the facts and studying the secondary causes.

Bacteriology.

Up to the time these lines are written the pathogenic microbe of typhus fever has not been discovered. We may note, however, the attempts that have been made in this direction. Hlava, of Prague, has described very minutely a streptobacillus met with in the blood of those dead of typhus fever. Kasan has found in the blood of the spleen in patients with typhus fever certain rounded bodies with filiform prolongations possessing movement; he calls them *Spirochetæ exanthematicæ*. He has found them quite constantly also in the blood drawn from the finger tips. Dubief and Bruhl described before the Academy of Medicine of Paris a microorganism, which they called *Diplococcus exanthematicus*, found by them in the blood of nine typhus-fever patients during the small epidemic occurring in Paris in 1892-93. They found it also in the blood in six bodies of those dead of typhus fever, and in the mucus of the nasal fossæ, the pharynx, and the larynx. Haushalter and Étienne, however, failed to detect this bacillus.

Le Gendre found a microbe resembling Eberth's bacillus in the blood of a typhus-fever patient during life, and in all the organs after the death of this person. Calmette believes that the microorganisms observed in the blood in typhus fever, and described by Hlava, Babes, Combemale, Bruhl, and Dubief are simply forms of one and the same bacillus described by Calmette himself, by Thoinot, and by Lewaschew.

In Mexico the investigations made by N. Ramírez de Arellano and I. Prieto have given no definite results. A veterinary practitioner, José L. Gómez, as the result of a series of investigations in the laboratory of the Superior Council of Health of Mexico, has come to the conclusion that the microbe which produces bovine typhus is identical with that of typhus fever in man.

Geographical Distribution.

Typhus fever occurs in endemic form in many different localities in Great Britain, and especially in Ireland; but throughout the United Kingdom it is manifestly disappearing, as the following figures show: In Ireland there were 505 deaths in the year 1885, and only 206 in

1891; in Scotland in 1871 there were 1,129 deaths, but in 1890 only 77; in England also the disease has markedly decreased. In many provinces of Russia typhus fever exists in endemic form. It is also endemic in Austria-Hungary, especially in Bohemia, Moravia, Silesia, and Galicia. The disease is likewise endemic in Germany, especially in the northern part. In Prussia typhus fever is gradually diminishing, as shown by the following figures: In 1878 there were 2,720 cases; this number fell to 1,193 in 1880 and to 174 in 1885. Typhus fever is endemic also in the Province of Algarve in Portugal. In Italy the diminution in the mortality of the disease is noteworthy: in the year 1888 there were 2,099 deaths from this disease, while in 1891 there were but 31. In France typhus fever persists endemically in parts of Brittany. As we have above remarked it reappeared in Paris in 1893, after having been absent eighty years.

In Asia typhus fever is said to be endemic in Persia and China. It has been reported, among other places in Africa, in Egypt, and we have already spoken of the endemic existing in the mountainous portion of Algeria and of the epidemic recrudescence occurring in the years 1866–68.

Coming to America, the frequent communication between England and Canada brought typhus fever to Quebec and Montreal on various occasions since 1820; and as a result of the great Irish emigration to the United States, the cities of Boston, New York, Philadelphia, and Baltimore have suffered from epidemics; but neither in the United States nor in Canada has the disease taken domicile in endemic form.

In the Mexican republic, as we have already remarked several times, typhus fever is endemic, and it will be interesting to consider briefly its geographical distribution in this country. Of the data at our disposal for the study of this question, we will mention only those of Dr. Ehrmann, contained in a very interesting communication[7] presented to the Academy of Medicine of Mexico on April 7th, 1866. They were the result of his own observations and those of the surgeons in the French army of invasion; it is upon these data that I shall base this study.

The republic of Mexico, as is well known, is bounded on the west by the Pacific Ocean, while on the east its shores are bathed by the Gulf of Mexico. From each coast the land rises gradually so as to form a tableland, which we have frequently referred to under the name of the central plateau of Anáhuac. The greater part of this tableland lies at an elevation of over two thousand metres (about six thousand five hundred feet) above the level of the sea. In it are found the principal cities of the interior of the country, where the population is most dense. Now in all this region typhus fever persists endemically

and presents frequent epidemic recrudescences of which we have already spoken. There are here more than twenty cities in which the disease hardly ever absolutely dies out; and even among the rural population typhus fever occurs quite often and is of considerable gravity.

Upon the slopes of the Cordilleras, and embracing the central zone on the east, the south, and the west, there is a region in which typhus fever occurs at intervals and in sporadic form. Epidemics there are rare and are usually imported. This zone includes the parts lying between the elevations of 1,000 and 2,000 metres (3,300 and 6,500 feet) above the level of the sea. Finally, in the coast region, along the shores of both seas, typhus fever is extremely rare.

This distribution presents a singular contrast which I cannot resist emphasizing. Along this coast, comprising the torrid zone of Mexico, is where yellow fever exists when it is imported from Vera Cruz or from the northern districts of the peninsula of Yucatan, the only points in which this disease is endemic. Yellow fever may develop along the slopes of the Cordilleras up to an elevation of one thousand metres above the level of the sea, but has never invaded the cities of the central plateau. It would seem, therefore, that the germ of yellow fever, whatever it may be, requires for its development climatic conditions, the opposite of those which the typhus-fever germ needs for its development.

The fact that typhus fever assumes the endemic form in Ireland, the poverty and sufferings of whose inhabitants are well known, the similar conditions under which live the inhabitants of Silesia, concerning which Virchow has spoken, and those which French physicians have described as existing in Brittany lead us to believe that insufficient food, want, crowding together in small and badly ventilated quarters, and physical depression are conditions favorable to the growth and development of the pathogenic germ of typhus fever. Similar conditions are met with among the lower classes inhabiting the poorest quarters of large cities, and also among people who have not received the benefits of civilization and who, through ignorance and poverty, violate the most elementary rules of hygiene, such as we see among the Arab tribes in Algeria (the Kabyles).

I shall not attempt to repeat the severe criticism to which each one of these circumstances that I have just mentioned has been subjected, and which has led writers on typhus fever to reject as causes of the disease all except overcrowding, physical and mental suffering, and ignorance of the laws of hygiene. These are conditions especially favorable for the development and epidemic propagation, but they do not cause it.

SECONDARY CAUSES.

The study of the secondary causes is of greatest interest and should not be omitted in considering the etiology of typhus fever.

Sex.—The statistics of fever hospitals in London, Dublin, Edinburgh, and Stockholm show that the two sexes are equally exposed to typhus fever. In Mexico, however, more women than men are attacked by this disease, as the following figures show: Of 8,581 cases of typhus fever reported to the Superior Council of Health from August, 1891, to the end of December, 1897, there were 3,952 men and 4,629 women.

Age.—As regards age I have made from the same sources the following table:

Age.	Cases.		
	Males.	Females.	Total.
Under 1 year	1	4	5
From 1 to 2 years	9	7	16
" 2 " 5 "	85	80	165
" 5 " 10 "	312	351	663
" 10 " 20 "	1,162	1,365	2,527
" 20 " 30 "	1,223	1,326	2,549
" 30 " 50 "	939	1,212	2,151
" 50 " 70 "	210	267	477
" 70 " 90 "	11	17	28
Total	3,952	4,629	8,581

In these figures we see that the disease is exceedingly rare in the first years of life; that it begins to occur with greater frequency between the ages of two and five years; that between ten and twenty years the disease occurs with four times greater frequency than before; that the morbidity is equally great between twenty and thirty years; that it begins to decrease between thirty and fifty; and that it falls more rapidly between the ages of fifty and seventy years, and still more between those of seventy and ninety. It should be noted, however, that the number of inhabitants between seventy and ninety years of age is very small in Mexico. From a comparison of these figures we learn that the period of life most subject to typhus fever is from ten to fifty years. Dr. Jiménez draws from his own observations the conclusion that typhus fever is most frequent between the ages of twenty and forty years, a conclusion which is in accord with our own figures.

Typhus fever does not attack recent arrivals in a region where it prevails endemically with the same frequency as does typhoid fever.

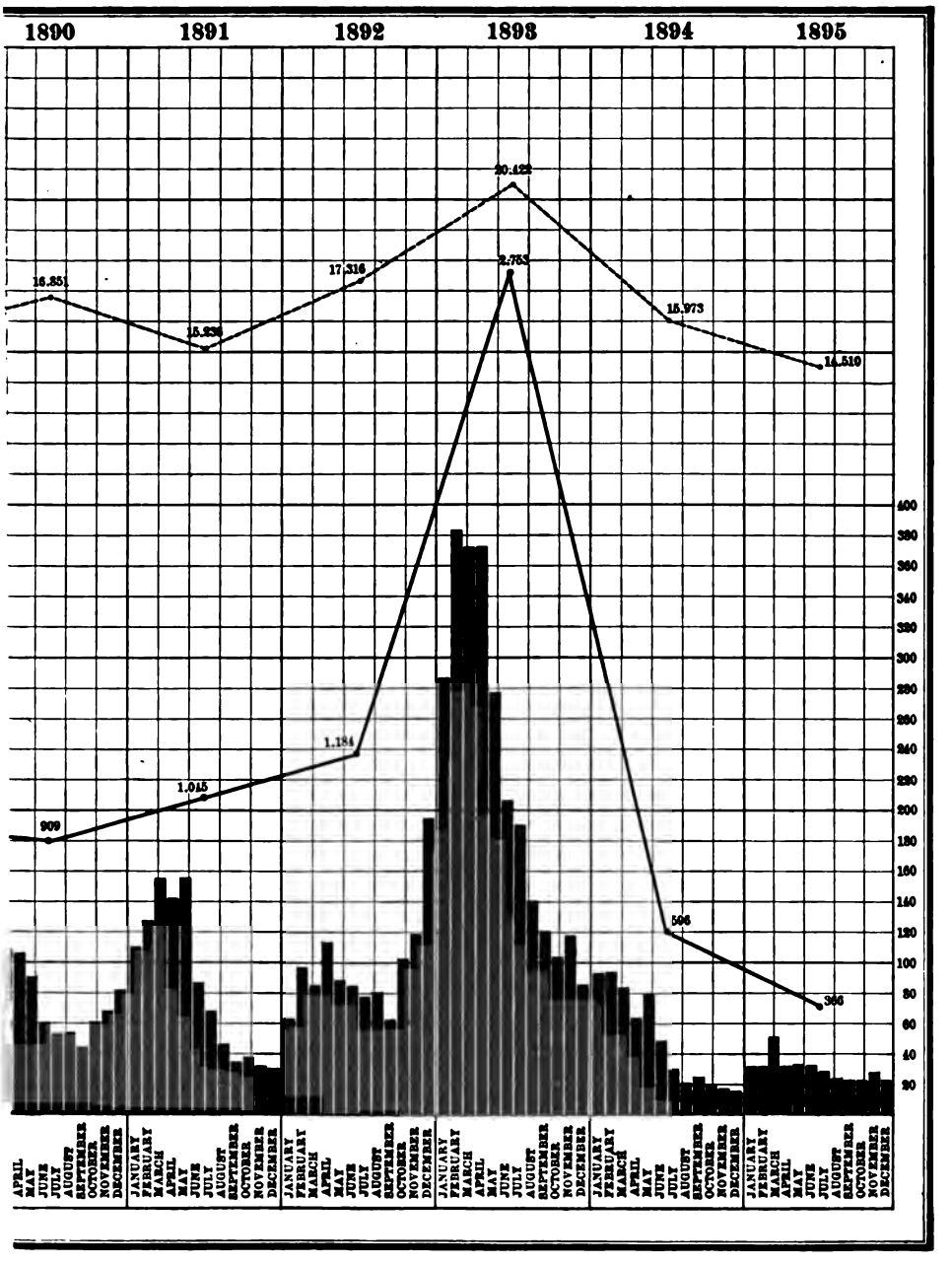
This same Dr. Jiménez, in an analysis of one hundred and sixteen cases, found only eleven in persons who had arrived in Mexico recently or who had been but a short time in the city.

Many European writers believe that typhus fever does not attack members of the upper classes, and the experience of Mexican physicians shows that the disease is more frequent among the very poor, which class is, as elsewhere, the most numerous; however, the disease does not spare altogether the upper classes, especially during epidemic periods.

One attack of typhus fever usually confers immunity, but this is not an absolute rule, as many authors have stated; I myself have records of numerous cases proving this fact. Indeed there are many accounts of second attacks; I remember, among others, that of a physician who had charge of the typhus-fever patients in the Hospital Juárez, and whom I saw three separate times suffering from typhus fever; another case which I saw was that of a lady who died while still young from a third attack of typhus fever.

Seasons.—The relation of season to the prevalence of typhus fever has been variously stated by different authors, but in general it is held that the disease occurs with greatest frequency in the winter and spring. This belief is confirmed by Hirsch's tables. Of 147 epidemics which have prevailed in the eastern and western hemispheres in temperate and cold regions and in which a record has been made of the date of appearance and the duration of the epidemic, 30 had their maximum in the spring, 21 in spring and summer, 19 in summer and autumn, 18 in the autumn alone, 17 in summer, and 14 in the autumn and winter, while they have ceased in summer (verano). The endemic in Mexico always increases in winter and during the dry season and declines as the rainy season comes on. In the City of Mexico the rains begin in June, increase during July, August, and September, and decline in October.

The annexed chart will give a more precise idea of the months in which typhus fever has usually increased, and of the epidemic which began in October, 1892, and continued until the summer of 1894, reaching its height in February, March, and April, 1893. In this chart the number of deaths during each month for the eighteen years is marked by the heavy vertical lines; the number of deaths for each year is joined to that of the following year by the continuous lines; and the number of deaths from all causes in each year is joined to that of the following year by the broken lines. As we see, the endemic remained almost stationary from 1878 to 1882; the number of deaths from typhus fever increased during the years 1883-84; decreased slightly, but remained almost uniform from 1885 to 1888; it


1890
1891
1892
1893
1894
1895
16.851
15.838
17.316
20.422
2.765
15.973
14.510
909
1.015
1.184
506
306
400
380
360
340
320
300
280
260
240
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APRIL
MAY
JUNE
JULY
AUGUST
SEPTEMBER
OCTOBER
NOVEMBER
DECEMBER
JANUARY
FEBRUARY
MARCH
APRIL
MAY
JUNE
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OCTOBER
NOVEMBER
DECEMBER

rose with epidemic exacerbations in the early months of 1889-90-91; and in 1892 began the epidemic which decreased a little up to September of that year, but increased in October, November, and December. The year 1893 was marked by the great epidemic which attained its maximum in February, March, and April, then declining rapidly to December, remaining at the same height during the first three months of 1894, returning to a simple endemic condition between June and December of that year, and being but very slightly elevated during the year 1895.

Most European writers attribute the exacerbation of the disease during the winter months to the fact that the people live then but little in the open air, but for shelter and protection against the cold shut themselves up in narrow apartments, badly ventilated, in which accidental crowding takes place. This is not the cause in Mexico, however, since the air is mild here; there is scarcely any difference in the seasons, and the mode of life of the people is the same in the winter as in the summer.

Among the occasional causes I should note, since it is mentioned by all Mexican writers, the fact that a person who is predisposed to the disease often acquires it after having been wet with rain, especially if this happens while he is fatigued. This cause is noted in two-fifths of the cases (Jiménez). We have endeavored to determine practically the truth of this assertion of Dr. Jiménez, and to this end charged the sanitary inspectors to make inquiry of the families of the typhus-fever patients whom they visited in the discharge of their duties, and to ascertain the cause assigned by them for the appearance of the disease in each individual instance. I have tabulated the data so obtained, but will not insert the table here since it contains much that is of no special interest as bearing upon the question which now occupies us. I will, however, extract from it the following figures: In 5,749 cases in which inquiry was made concerning the cause of the disease, the following answers were obtained: Contagion, 1,686; infection, 1,108; catching cold, 2,058; a wetting, 570; exposure to the sun, 327. These figures were obtained in the following way: If the patient had been in contact with one or more persons ill with typhus fever shortly before he himself fell ill it was said that he acquired it by contagion. If this mode of transmission was not evident, if in the house occupied by the patient or in which he was when he contracted the disease, the water-closets were in a bad condition and gave out a bad odor, or if the drains were stopped up, or if from any other cause there was an accumulation of fecal matter, or even if the patient had breathed in the emanations from an uncovered drain, or from matters which had been taken from the sewers and exposed to the air,

then it was said that the disease was acquired through infection. We have desired to retain these expressions which are used not only by the laity, but by most physicians in Mexico, in order not to deprive the results of this investigation of their character of originality, in that they show that the acquisition of typhus fever through contact with or proximity to the sick is a little more frequent than is the other mode, which we have called infection. Under this head, without denying that contagion may sometimes have occurred in addition to inhalation of the gases which are given off from fecal matters in process of decomposition, the fact is simply noted that the person was exposed to these emanations. The number of cases acquired through contagion was 1,686, while that of cases through infection was 1,108. Imperfect as are these data, they nevertheless possess much interest, and when this method of collecting them shall have been perfected they will be of undoubted utility.

The number of cases ascribed to catching cold was 2,058. Here there has been an evident confusion as to the causes of the disease, for the laity may make such statements according to their own observation, free from all preconceived ideas; we, in analyzing these facts, regard the two first as efficient causes, that is to say true causes of typhus fever, while the third, catching cold, is merely an occasional cause. There is no antagonism between this and the two first mentioned, for a disease contracted through contagion may have cold as an occasional cause. A cold which produces sudden disorder in the nervous system leaves the organism momentarily without defence and during this period infection occurs. Catching cold through a drenching, as by a sudden shower, for example, is a special mode of catching cold, especially if it occurs after exercise in the sun or while the person is fatigued. This will explain the three occasional causes given in the above enumeration under the name of catching cold, wetting, and exposure to the sun; these three together give a total of 2,955 cases. Thus we see that out of a total of 5,749 cases of typhus fever it was stated that the occasional cause was catching cold in 2,955, that is to say, in 51.4 per cent. We see then that catching cold is a well-established occasional cause of typhus fever, and this is a fact which has an important bearing on prophylaxis.

Pathological Anatomy.

About the middle of the present century the memorable writings of Louis, Andral, Bouillaud, and Chomel sought to explain the various pyrexias by the facts revealed at autopsy, and they defined perfectly the characters of typhoid fever, which was the one that those

French physicians were able chiefly to observe in their hospitals; but our clinicians confounded this affection with typhus fever, believing that they were but two varieties of one and the same disease. Gerhard of Philadelphia and Shattuck of Boston published important works upon the differential diagnosis of these two diseases.

Unaware of these investigations, a distinguished Mexican clinician, of whom we have already had occasion to speak, Dr. Miguel F. Jiménez, devoted himself to a very careful study of the pathological anatomy of typhus fever, as a result of which he was enabled to demonstrate that the anatomical lesions of the fever observed in Mexico were different from those of typhoid fever.*

Nervous System.—In the cerebral meninges we find a very marked congestion of the pia, extending sometimes to the choroid plexus, producing in it sanguineous infiltrations in the interstices of the cellular tissue. There is always found a subarachnoid effusion, sometimes turbid, at other times transparent, sometimes reddish, and again yellowish; in some or all of the cerebral ventricles there is a serous effusion, usually clear, but occasionally sanguinolent. On section of the cerebral substance the white surface is found to be dotted with numerous red points which are seen to be minute drops of blood.

In the spinal meninges we always find injection of the pia with subarachnoid effusion.

These findings are not the result of cadaveric hypostasis, since they are not always in the most dependent parts and since they are also found at autopsies made a very few hours after death. They cannot be attributed to asphyxia, since typhus-fever patients do not die asphyxiated. Finally, they do not present the characters peculiar to meningoencephalitis.

The *respiratory apparatus* presents constant lesions. In almost every case we find congestion of the posterior portion of the lungs, which is to be distinguished from hypostatic congestion and resembles more exactly the condition which has been called splenization by the French; the lung has lost its elasticity, contains little or no air, does not crepitate when squeezed, and the liquid thus expressed is not frothy. In seven out of twenty-one cases there was more or less extensive pneumonia present. It is very rare to find evidences of pleurisy; the effusion, when it exists, is serous and limpid.

The nasal fossæ and the pharynx are dry and red. The trachea and bronchial tubes are of a very dark color, the lining membrane is notably softened and covered with adherent mucus.

In all autopsical reports more or less explicit mention is made of the condition of the *heart*. The endocardium is frequently reddened.

The myocardium is flaccid and appears withered and shrunken, and we frequently find evidences of myocarditis.

The Blood.—As at the time when these first observations were made recourse was had more frequently than now to venesection, it was possible to study the condition of the blood during the life of the patient. In the observations which Dr. Jiménez made the blood was stated to be fluid and with but little tendency to coagulation; it resembled in some cases "a watery fluid holding in suspension a very fine powder of a dark red color," in other cases it resembled "the blood of a scorbutic patient," and at another time "serum mixed with snuff."

An accident which has been observed in Mexico is gangrene of the lower extremities, following thrombosis of the main arteries. Phlebitis of the lower extremities has been noted a number of times. Cicatrices are sometimes observed over the sacrum and at other places where pressure occurs.

Microscopical examination shows in the heart, muscles, kidneys, and liver changes analogous to those occurring in other fevers, especially in typhoid.

The *stomach* is sometimes reddened, either in disseminated points or over a large area of the splenic extremity. The rest of the mucous membrane is of a slate color; sometimes there are ecchymoses and a more or less extensive softening.

The *intestinal lesions* are of great interest, for they have served more particularly to distinguish typhus from typhoid fever. In the latter disease Peyer's plaques are enlarged, hardened, or ulcerated, the ulcer frequently involving all the coats of the intestine and sometimes resulting in perforation, with consequent peritonitis from effusion of fecal matter into the peritoneal cavity. The ulcers are also the cause of the intestinal hemorrhages, which aggravate so greatly the prognosis of typhoid fever. In typhus fever nothing of this sort is observed. Usually there is injection of the mucous membrane in the form of branching lines. Jiménez observed in the lower portions of the small intestine spots of a grayish color and of oval shape, and the more often confluent the nearer they were to the cæcum. This observer likened their appearance sometimes to that of wet parchment, at other times to that of the not too recently shaven chin, and believed that they were formed of a large number of pyramidal granulations. They were neither hard nor raised above the surface nor were they ever the seat of ulceration. They were thus easily to be distinguished from the lesions of typhoid fever, which we have just described.

Another change which is commonly met with is in the isolated

follicles of the small intestine, but these lesions are never of the size or consistence nor have they any other of the characteristics of typhoid lesions.

The mesenteric glands are swollen and more or less congested, but never present any signs of inflammation or of suppuration, as we see commonly in typhoid fever.

Incubation.

The time that elapses between the moment that one is exposed to the contagion of typhus fever and that at which the disease begins is called the period of incubation. This period varies with the degree of virulence of the germ, that is to say, the vitality of the seed, and according to the condition of receptivity of the organism, that is to say, the richness of the soil. This explains the differences in the statements of certain observers of equal authority and credibility, such as Murchison in London, Theurkauff in Göttingen, Virchow in Berlin, Rosenstein in Gröningen, Behse in Dorpat, and the Mexican physicians. The average duration is twelve days, but as I have already shown it may be much less. Murchison declares that the duration of the period of incubation was five days when he himself contracted the disease. I have previously mentioned a case in which the period was three days, and I have other well-authenticated reports of cases in which it was even less, and in one instance the onset of the disease may be said to have instantaneously followed exposure. The duration may be greater than the average just stated, even up to twenty days. In the ships which brought back the soldiers, both the well and invalided, from the Crimea, instances were noted in which twenty, fifty, and even sixty days had passed after the last exposure to typhus before the disease appeared. As very many persons were attacked simultaneously, no cases being noted previously, it could not be maintained that the germs of the disease had been preserved by transmission through a number of successive cases.

When the microbe of typhus fever shall have been discovered, many of these uncertainties will be explained, but at present we must content ourselves with one of two explanations. The first of these is that the germ was carried by the soldiers themselves, but remained innocuous until a change in the condition of the individual converted the soil into a fit medium for the evolution of the microbe. Take, for example, the 64th Regiment which embarked at Balaklava on April 29th; it arrived at Marseilles on May 10th, and at Villefranche by rail on the 12th; on the 16th it reached Chalon-sur-Saône, where it was detained four days by a flood; on May 24th the first case of

typhus fever was declared, and other cases quickly followed. It is possible that the soldiers brought the germ with them, and while they travelled in ship or by rail they felt no effects from it; but when they began to march on foot, suffering fatigue, and especially when they were drenched with rain, the organism became converted into a favorable soil for the development of the microbe.

Another explanation is offered of those cases in which persons who have been exposed to the contagion of typhus fever have not contracted the disease themselves but have communicated it to others. The explanation is that the germ may be transported in the clothing and may preserve its virulence for a long period. In support of this theory we may recall the case above related in which some underclothes, which had been used by a patient with typhus fever, were kept for eight months and then infected the two sisters of the patient who began to wear them after this period.

I believe, therefore, that these cases of seemingly very prolonged incubation are really not such, but may be explained in the way above indicated.

Symptoms.

The symptoms of typhus fever are similar to those of any other infectious disease, but they group themselves in such a fashion, succeed each other in such an order, and appear usually at such precise periods that they give to the affection a special physiognomy which serves to distinguish it clinically from all other diseases.

The invasion is sudden, without prodromes. The disease begins ordinarily with a chill, followed by pain in the head, lassitude, muscular fatigue, and general malaise. The temperature rises rapidly, reaching 39° or 40° C. (102.2° or 104° F.), and remains there with slight oscillations. The patient soon feels unable to work, and gradually experiences difficulty in standing or sitting erect by reason of the vertigo; then follow rapidity of pulse, heat of the skin, dryness of the mouth, thirst, anorexia, dark colored and scanty urine, and all the array of symptoms which always accompany high fever. Constipation occurs in nine-tenths of all cases (Jiménez). Insomnia is an early symptom and persists for many days. The first four days of the disease are characterized by the symptoms of intense fever among which cephalalgia, insomnia, vertigo, and muscular fatigue predominate. One episode only interrupts the uniformity of the symptoms, and that is epistaxis which appears on the third day. On the fifth day appears an eruption on the skin, which stamps the disease with a special seal. Small spots of a reddish color, more or less dusky, come out first on the chest, then on the back, and finally on

the upper and lower extremities. The first day these are usually few in number and not very conspicuous, but from the following day they increase in number and become more deeply colored; they disappear on pressure by the finger. On the succeeding days they grow more and more dark in color, and finally do not disappear under pressure; the eruption has become petechial in character.

The disease is now characteristic in its appearance. The symptoms become daily more marked. The patient exhales a bad odor, the skin is hot, the face is red, the conjunctivæ are injected, the patient has difficulty in opening his eyes, the face is slightly swollen, and in general the expression is dull and stupid, resembling that of a drunken man (Jiménez). The headache, always very intense, persists up to the eighth day, and then begins the peculiar delirium of typhus fever; the lips move as if the patient were speaking in a low voice or were talking to himself; if he is spoken to his attention is attracted, but perception is slow, although the patient will answer correctly the questions that are put to him. Now he begins to suffer from deafness and noises in the ears, and from a trembling in the limbs; he becomes giddy if only he attempts to move in the bed or to raise his head. At this time also is noticed a tendency to remain in the dorsal decubitus. As time goes on, in the course of the second week, the morbid picture becomes more marked; the scene does not change, but the symptoms all become aggravated. A heaviness and weight in the head succeed the cephalalgia, the delirium is more intense, and the insomnia persists. The patient lies upon his back, with the mouth half open, the lips separated, the teeth dry and covered with sordes, the tongue dry, blackish, and hard, like a parrot's. The abdomen is tense and slightly tympanitic, and constipation persists. The bladder becomes paralyzed and the urine gradually distends it until it has reached the limit of its elasticity, and then if the situation is not relieved by the use of the catheter, the sphincter relaxes, and the urine dribbles away without the patient's knowledge. If, as sometimes happens, diarrhœa sets in towards the end of the disease, the fæces are passed involuntarily and unconsciously. As the days go on the skin becomes almost wholly discolored with the eruption, the face grows livid, the nostrils are dry and scurfy; the pulse is frequent and small, and at times intermittent; the temperature rises still higher, carphologia sets in, and the drowsiness may go on to coma.

If the attack is to terminate fatally all the symptoms increase in severity, and the patient dies exhausted, if the disease is of the adynamic form; or with agitation and more or less furious delirium, if the affection has assumed the ataxic form.

If recovery is to take place, the temperature falls rapidly from the fourteenth day; sleep comes to the patient, and upon awakening he feels refreshed as if he had really slept for a long time. In place of the indifference to all his surroundings, which had hitherto characterized the patient, succeeds an interest in knowing what has happened. The mouth becomes moist, the tongue cleans, appetite returns, and thirst diminishes. If the eruption has not already become paler, it now begins to lose its color, the petechiæ fade, and the skin becomes soft and moist. The pulse diminishes in frequency and gradually regains its former strength and fulness. The deafness and a certain degree of stupefaction still continue, but the alarming nervous symptoms disappear, a sense of muscular fatigue, slowness in movement, and great debility alone persisting. Recovery is much more rapid than in many other infectious diseases, provided the attack has not been of unusual severity or of very long duration.

This is the picture of typhus fever as it occurs in the city of Mexico. The disease presents the aspect of an infection but with certain characteristics peculiar to it, such as the sudden onset, the initial chill, bleeding from the nose on the third day, the characteristic eruption on the fifth day, the predominance and the precocity of the cerebral symptoms, the frequent presence of constipation, and the cyclic march of the disease.

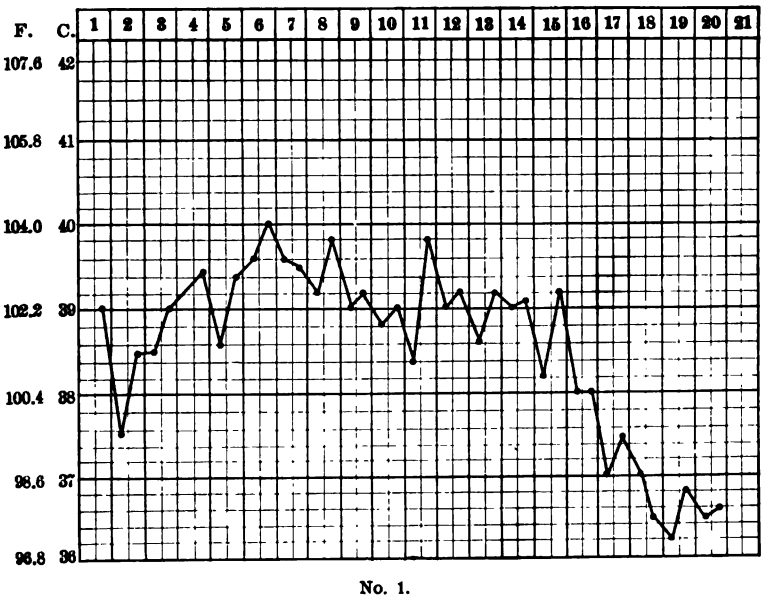
We will now study each of the symptoms in detail, noting the modifications which it may undergo.

Invasion.—We have said that typhus fever begins usually in the midst of health with a more or less intense initial chill. This is the rule established by the study of one hundred and three cases in which Jiménez was able to inform himself concerning the commencement of the attack,* although there are other cases on record in which the disease began during the course of a bronchitis, of a gastrointestinal affection, or more commonly of intermittent fever.

In the early days of the attack the fever may present remissions or even intermissions. These may be explained by an individual peculiarity or by association with malaria which is very frequently observed in Mexico.

Headache.—In the one hundred and forty-seven cases which form the first series studied by Jiménez this symptom was not absent in a single instance, and it has never failed in any of the cases which I have observed. It is located usually in the frontal, supraorbital, and temporal regions and in the eyeballs. In cases in which it has been possible to determine with accuracy the duration of this headache it has usually been found to be eight days. The pain in most cases is so severe as to form the patient's chief complaint.

Epistaxis.—We have constantly observed this symptom on the third day in cases in which the exact beginning of the disease has been known, but as other observers have met with it on the fourth or fifth day or even later I must admit that it may occur at that time. The bleeding from the nose may recur two or three times in the course of the disease. Sometimes there may be only a few drops of blood and it is necessary to be aware of this fact, since ignorance of it may lead to error; many patients of whom I have inquired whether there has been any nose-bleed have replied in the negative, although

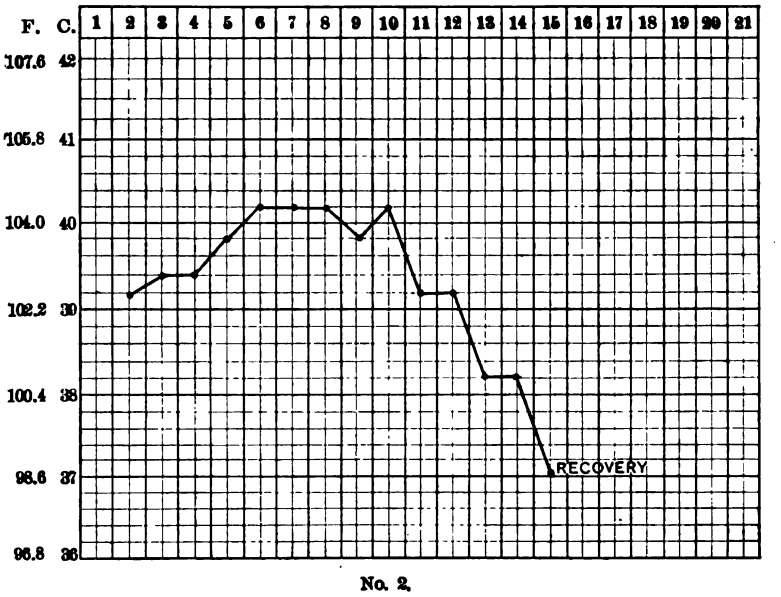


No. 1.

at the very time I noticed one or two drops on the pillow or sheet. At other times the hemorrhage may be very profuse and in one case noted by Jiménez it was the cause of death.

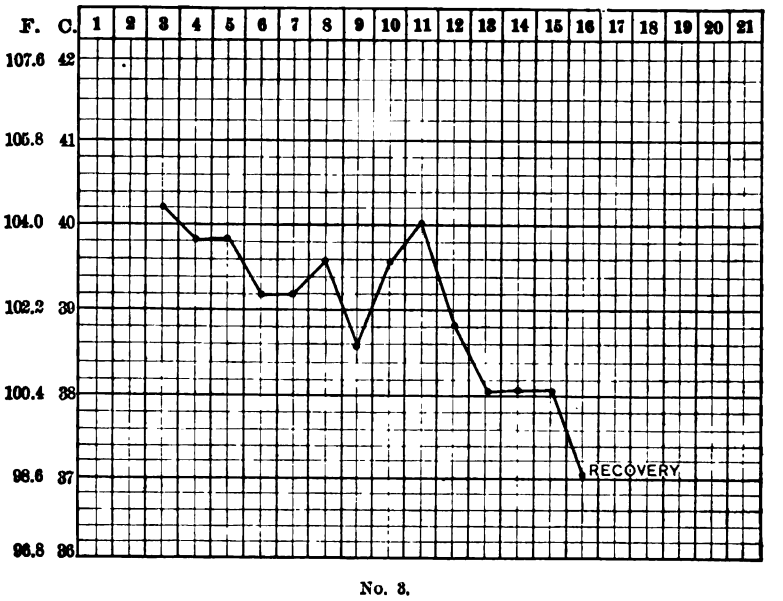
Fever.—This resembles, as I have already said, the pyrexia of other grave infectious diseases, but it is peculiar in that it rises rapidly from the very onset of the disease. After it has reached about 40° C. (104° F.) it remains at this height with slight oscillations above and below it. When it begins to decline its fall is rapid, but not so rapid as was generally believed before the use of the thermometer enabled us to appreciate its exact course. In cases of favorable termination, the temperature begins to fall between the ninth and eleventh or twelfth days; exceptionally the fall begins earlier, or, more commonly, on the thirteenth day or later (Jiménez). In the majority of the cases which I have observed defervescence began on

the fourteenth day. When the fever lasts more than fourteen days its descent is more rapid. The accompanying charts, for all except the



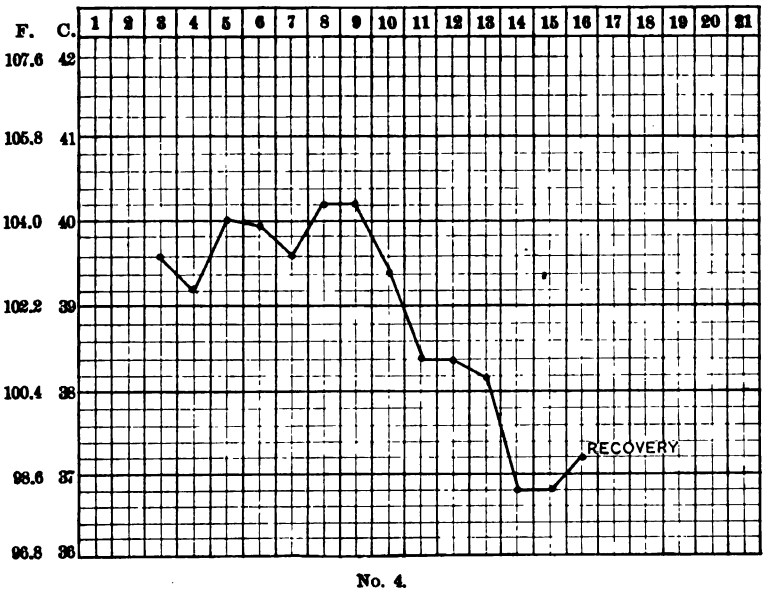
No. 2.

first of which I am indebted to Dr. J. M. Lugo Hidalgo, will give an idea of the usual course of the temperature.



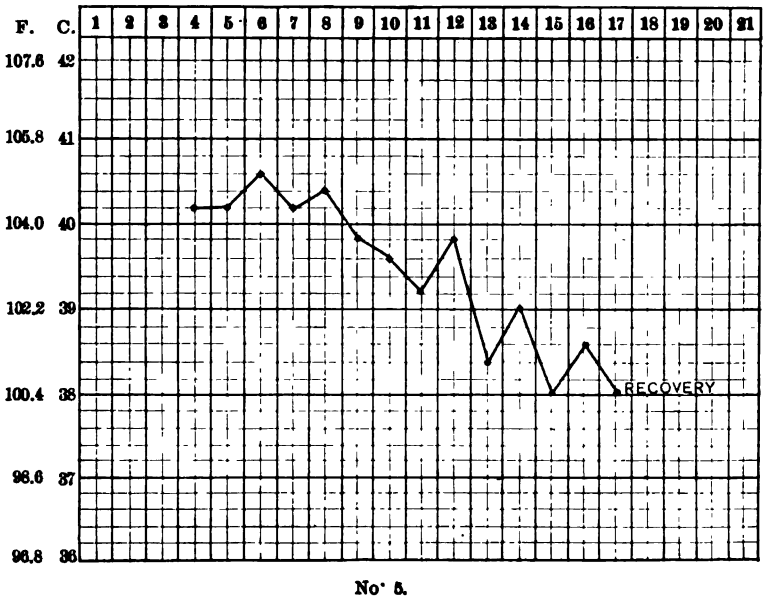
No. 3.

No. 1 is that of a medical student in the last year of his study, vigorous and in good health, in whom the temperature could be taken



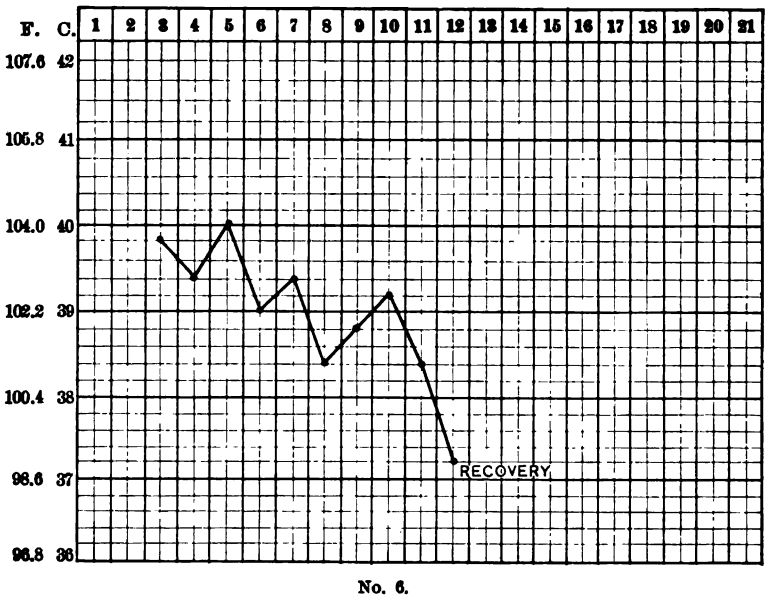
No. 4.

every two hours. It presents the following peculiarities: On the morning of the second day there was a very marked remission, which



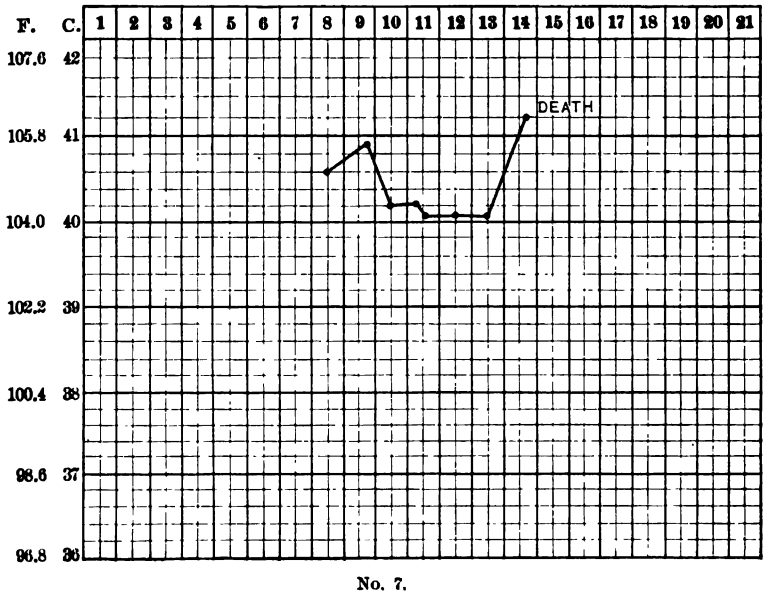
No. 5.

led us to think of intermittent fever; on the morning of the fourth day the remission was so marked that the patient believed that he



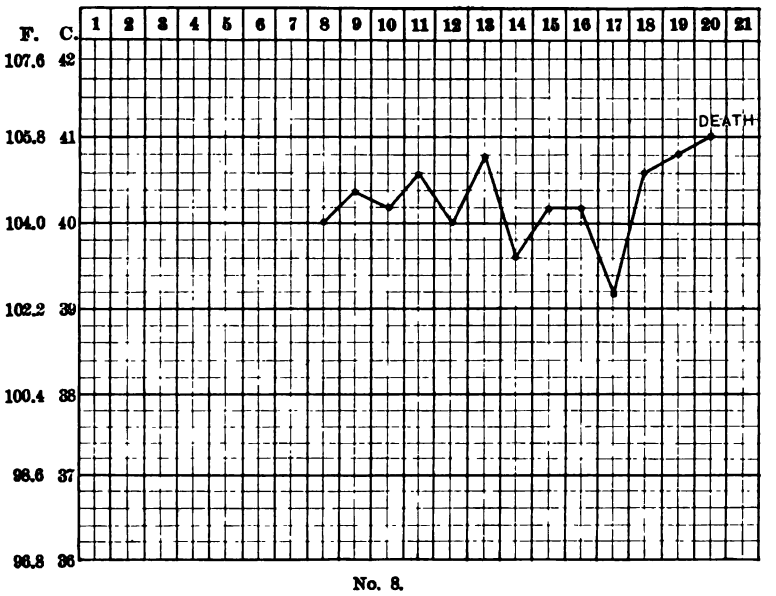
No. 6.

was well and did not use the thermometer, for which reason there is an interruption in the tracing. It is to be noted that when the ther-



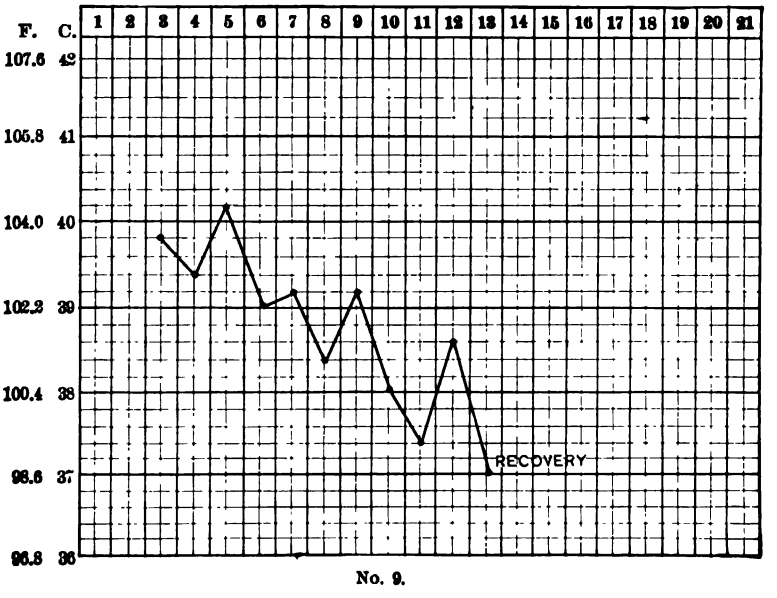
No. 7.

mometer marked 40° C. the attending physician prescribed 15 to 20 cgm. (2¼ to 3 grains) of antipyrin.



No. 8.

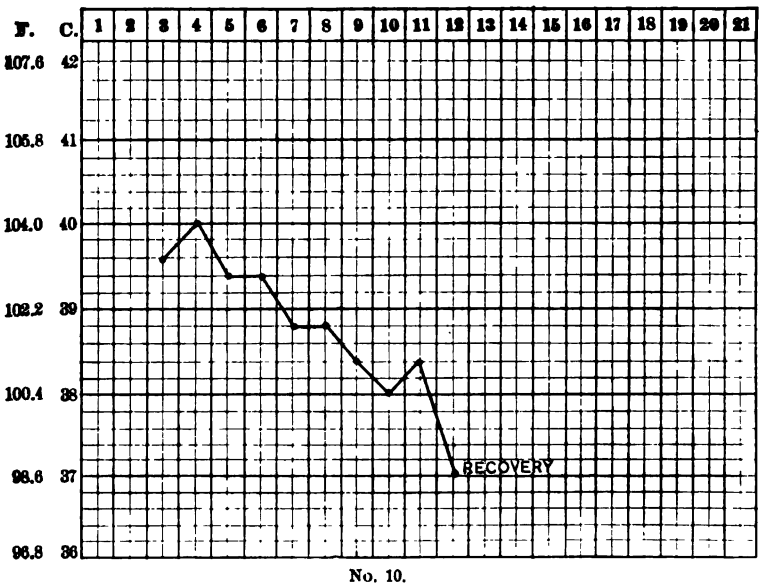
Chart No. 2 is that of a woman, forty years old, of good constitution, who suffered from the ataxo-adynamic form of typhus fever.



No. 9.

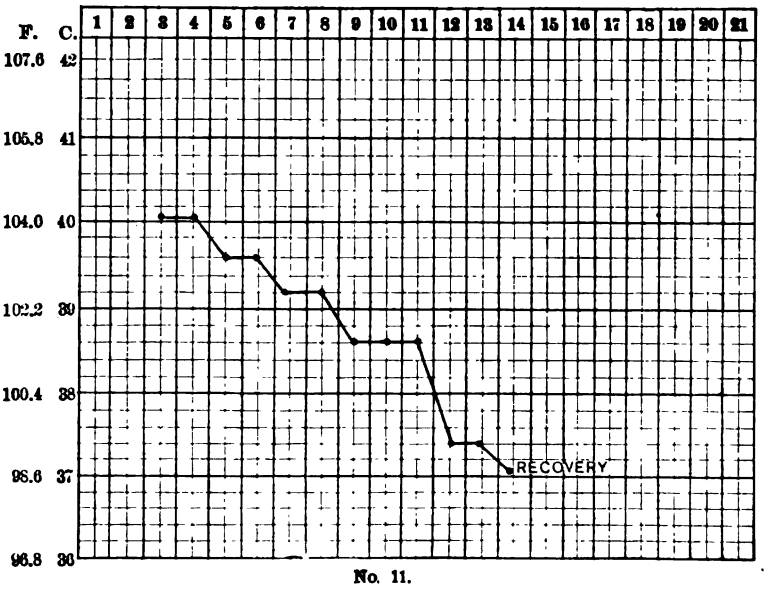
This tracing represents one of the frequent types of the temperature curve of typhus fever.

No. 3 is that of a woman, fifty-three years old, with a mild ataxo-



No. 10.

adynamic form. There was an exacerbation on the eleventh day and from that time the fall of temperature began.



No. 11.

No. 4 is that of a young man, twenty-one years old, healthy, but of the lymphatic constitution; he suffered from the adynamic form of typhus fever; the fall began on the ninth day.

No. 5 is that of a woman, fifty years old, of good constitution, suffering from the adynamic form.

No. 6 is a type of the temperature curve of benign typhus; it is that of a woman, twenty-eight years old, of moderately good constitution and lymphatic. In all these cases the disease terminated in recovery. The two following charts are those of fatal cases of typhus fever.

No. 7 is that of a woman, sixty-seven years old, of bad constitution, and alcoholic; she suffered from a very severe attack of the adynamic form, and died on the fourteenth day.

No. 8 is that of a woman, fifty-nine years old, of poor constitution, physically and mentally depressed; she died on the twentieth day. These two charts show also the grave course that typhus fever follows in persons advanced in years, in whom death is the most fre quent termination of the disease.

In contrast with these two, Chart No. 9 is that of a young man, fifteen years old, of good constitution, who passed through an attack of benign typhus, terminating on the thirteenth day.

No. 10 is that of a child, ten years old, of lymphatic constitution, in whom the disease took the adynamic form.

No. 11 is that of a child of eight years, of good constitution. This attack of typhus fever terminated in recovery on the fourteenth day. In these cases the disease terminated in recovery, which is most frequently the case in children.

Pulse.—The frequency of the pulse in typhus fever is almost always in direct relation with the temperature and with the frequency of respiration, but if the respiratory organs become involved, this ratio as regards the respiration is altered. The ratio between the temperature and the pulse rate is modified also when there is a complication affecting the circulatory apparatus, especially the heart. Such a disproportion is a sign of bad omen. Intermittency, irregularity, and smallness of the pulse possess the same signification as they do in diseases of the circulatory apparatus, but they are all signs of greater gravity of the attack.

Exanthem.—The eruption on the skin appears always on the fifth day, according to my observations, but other physicians have noted its appearance on other days from the fourth to the seventh. Murchison noted it on the fourth and fifth days, Jiménez from the fourth on, but never later than the eleventh, and Terrés on the sixth day. Jiménez never found it absent in any of his observations. Murchi-

son failed to discover it in fifty-five cases out of two thousand four hundred and ninety studied by him.

The eruption begins on the chest and abdomen, according to Berruecos most frequently on the shoulder; it extends, as we have said, over the rest of the body and then over the upper and lower extremities. It is ordinarily not very abundant on the first day of its appearance, but becomes confluent on the following days and sometimes covers almost the entire body. It appears sometimes as wheals but more often as patches, resembling those of measles. In color it varies from pink to wine red. At first it disappears like all the exanthemata under pressure of the finger; later there appears in its centre a point of more dusky hue which does not disappear under pressure, and finally the whole patch acquires this character, the eruption becoming petechial in its nature. In certain grave cases the exanthem is petechial from the beginning, while in other cases the eruption does not assume a petechial character at any time during the course of the disease.

Jiménez marked certain of the patches with nitrate of silver, and in this way was able to determine the duration of each crop to be from six to ten days.

During convalescence there is a furfuraceous desquamation following the eruption, as I have observed in a multitude of cases, although Jiménez asserts that he has not seen it.

Nervous Symptoms.—I have remarked above that the symptoms on the part of the nervous system are distinguished by their precocity and their constancy. I have spoken of cephalalgia and insomnia. The latter is almost constant, very difficult to overcome, and usually lasts throughout the whole course of the disease. Hyperæsthesia of the skin is frequent and marked, and begins as early as do the muscular pains. Vertigo is also very constant and very precocious, and appears, as I have said, when the patient attempts to stand on his feet, to sit up in bed, or even to raise his head. Stupor is most characteristic of the disease, and, indeed, it is to this symptom that typhus fever owes its name, this word (τῦφος) being employed in ancient medicine to designate stupor. The term embraces a number of the symptoms which we have already mentioned, such as somnolence, a dull expression, weight in the head, and stupidity, all of which are always present. The intelligence becomes gradually more and more dimmed, perception is slow, replies to questions, although given, are tardy, the memory is gradually lost, and the patients cannot tell what the day of the week is nor the month. It seems to be a labor to them to think. But in contrast to their indifference to their surroundings and the slowness of external perceptions, the internal activity is very

marked; the patient is sometimes delirious from the first days of the disease and is almost constantly so in the second week.

This delirium demands a few words; it is the expression of this interior activity of which we have just spoken. Sometimes it is what the French have called typhomania: the patient speaks incessantly in a low voice or between his teeth, scarcely moving his lips; if his attention is attracted, he awakes, answers more or less unwillingly, and then renews his soliloquy. At other times the delirium concerns itself with the business of the patient, his inclinations, or his habitual preoccupations; he attempts to go to his work, to his office, to fulfil a commission with which he had been charged, or to consult on business matters; he rises up in bed, looks about for his clothes, sometimes he even gets out of bed and walks a few steps, but falls worn out with excessive fatigue, which is even out of proportion to his actual debility. The delirium may be furious in character; the patients are agitated, they struggle and make an exhibition of strength of which we did not believe them capable. It is usually in the ataxic type of the disease, in young and vigorous patients and in alcoholics, that the delirium assumes this form. In the alcoholics we may see true delirium tremens.

The vacillating movements, the trembling of the limbs, the carphologia, the paralysis of the bladder with involuntary micturition, and also the involuntary discharges from the bowels are frequent and grave symptoms.

The somnolence and stupor may merge into coma. The signs of adynamia, when this is the form the disease assumes, go on increasing during the course of the malady until the patient's strength is exhausted.

In the final stage of typhus fever symptoms of involvement of the great sympathetic are added to those referable to the central nervous system.

Digestive Apparatus.—We have already said that the symptoms on the part of the digestive organs present nothing characteristic, if we except the constipation which is observed in nine-tenths of the cases; in the remaining tenth of the cases we find involuntary evacuations or diarrhœa, which latter may sometimes be very profuse. Meteorism is observed during the second week or even earlier, if care has not been taken to evacuate the bowels.

Cardiovascular Apparatus.—Typhus fever, like all the infectious diseases, gives occasion to secondary infection of various organs. We have mentioned in the section on pathological anatomy the frequency of changes in the endocardium, the myocardium, and the large vessels. The symptoms of myocarditis are the same as thos

of this malady when it occurs in the course of other infectious diseases, and we have mentioned above the changes which the pulse may present in such cases. The symptoms of disease of the circulatory apparatus, even when they cannot be regarded as peculiar to typhus fever, aggravate extraordinarily the prognosis, since they are often the cause of death.

We may attribute to secondary infection the thrombosis of the veins of the lower extremity manifested by the symptoms of phlegmasia alba dolens. Arterial thrombosis appears to be more frequent in Mexico than it is in Europe, and it causes gangrene of the toes, of the leg, or even of the entire lower extremity. Dr. José Ramírez, who was chief of clinic in 1875, has informed me that he made many autopsies in cases of typhus fever in which death had occurred as the result of gangrene of the leg, following a generalized arteritis of the femoral and tibial arteries. Gangrene was a frequent complication of typhus fever during that year.

In the epidemic of last year typhus fever was complicated with parotitis, which sometimes ended in suppuration and caused death after the patient had entered into the period of convalescence. Another complication observed in this same epidemic was noma, or the water canker of children.

Respiratory Apparatus.—On the part of the respiratory organs we observe dryness of the nasal mucous membrane and swelling of that of the pharynx and bronchial tubes; but there is nothing characteristic in this, such as we see in typhoid fever. We find symptoms of congestion of the base and posterior portions of the lungs, the presence of which we referred to in the section on pathological anatomy, explaining it by the supine position maintained so persistently by the patients in typhus fever. Pneumonia, which is found so frequently at autopsy, is not always manifested clinically by the symptoms peculiar to this condition; it may acquire a great intensity in consequence of the malignant character which all inflammations are prone to assume in the course of typhus fever.

Urinary Apparatus.—European observers have noted disease of the kidneys in typhus fever. Murchison met with it in seventy per cent. of his cases. It is seen also in Mexico, but I am unable to give any statistics as to its frequency. In former times the urine was examined only as regards its external appearances, but since the results of analysis of this fluid have demonstrated what valuable information it may give us as to the condition of the internal nutritive processes, it has been resorted to in most febrile diseases. But the comparatively short time during which this procedure has been employed in typhus fever has prevented me from collecting very numerous statis-

tics, and in this study I shall make use only of those furnished me by Dr. José D. Morales, professor of pharmacy in the School of Medicine in Mexico. In two hundred analyses which he made of the urine in typhus fever he observed the following: The urine is concentrated, as in all febrile diseases, and is more highly colored than normal; its specific gravity is always increased, sometimes reaching 1.033; its proportion of solid constituents is in relation to its concentration and density; among the solid contents the organic predominate over the mineral. The proportion of urea is always increased, as in all febrile diseases, and the same is true of the uric acid. Albumin is frequently found. Peptone and urobilin are present in the urine, and we also observe the biliary acids and pigments. On the fifth day of the disease we may find hyaline casts and pigment granules. The phosphoric acid is increased in proportion to the urea, and the chloride of sodium is diminished in amount. These data accord with those obtained by Dr. Luna y Drusina, chemical analyst of the Superior Council of Health of Mexico.

Course and Duration.

Course.—The picture which we drew at the beginning of the section on symptomatology is that presented by typical cases of typhus fever, and the reader is referred to it for a description of the normal course of the disease. But this type may not only be modified in different epidemics and in different countries, but it may even assume a local color in the different communities in which it prevails endemically. Sometimes it follows a rapid course: the symptoms succeed each other swiftly, and the gravity of the affection is so augmented that by the end of the first week it has reached its height. In other cases the symptoms develop slowly, they do not possess a grave character, nor do they assume it except in those cases in which the disease terminates fatally. Between these extremes there are all gradations passing almost imperceptibly from the course of the typical attack, which we described at length in the previous section, to any of the modifications to which we have just referred.

Duration.—Dr. Jiménez, from a study of all his cases in which he was able to determine the precise moment of onset, arrived at the conclusion that in a little more than two-fifths of the cases the disease terminates on the fourteenth day, but this termination is accelerated one or two days, or is retarded a like period, in about one-sixth of the cases. A few patients get up at the end of the third week, and fewer yet pass into the fourth week. The same author says that those cases in which all the stages of the disease are passed through

in the course of the first week deserve the name of fulminant. Murchison also concludes, as a result of his investigations, that the ordinary duration of typhus fever, when no complications occur, is thirteen or fourteen days.

Varieties.

Following the usual custom of all writers I shall enumerate the different forms or varieties which typhus fever may present in its course, but without regarding them as more important than simple modifications which any disease may assume in relation with the individuals whom it attacks or with the greater or less intensity of the symptoms determined by it. I do not think that the employment of these terms contributes to the advancement of science, but since they have been used by various writers it is necessary to know them. They are as follows:

Inflammatory Typhus.—This form is seen in young and robust individuals and is marked by high temperature, heat and redness of the skin, intense headache, and acute and early delirium.

Ataxic Typhus.—This form is characterized by an exaggeration of all the symptoms depending upon involvement of the nervous system, such as somnolence, delirium (which in these cases is very marked, violent, and even furious), trembling of the limbs, subsultus tendinum, carphologia, etc.

Adynamic Typhus.—This form is characterized by the early appearance of symptoms indicating debility, such as fatigue, prostration, cardiac weakness, involuntary discharges, paralysis of the bladder, etc. In this form it is observed that the skin loses its elasticity and pits on pressure with the finger. Collapse, of which we have already spoken, is frequent in this variety of the disease.

Ataxo-Adynamic Typhus.—This name is given to a combination of the two forms just mentioned and is a very common variety of typhus fever, Barralier having found it eight hundred and ten times out of thirteen hundred cases.

Many other forms have been described, but in my opinion they are unimportant, the three above described forms being those which give to the disease its peculiar and characteristic expression.

Complications.

We shall not attempt to describe here all the complications which may be encountered during the course or at the termination of typhus fever, but merely those which by their frequent occurrence constantly attract the attention of the physician and impose upon him the obligation of making a careful examination each day of the condition of all the organs, in order to prevent, by timely treatment, any untoward results.

Circulatory Apparatus.—Among the lesions of this system I may mention cardiac weakness and a disproportion between the pulse rate and the temperature, which latter gives warning, not only of dynamic disturbance of the heart and vessels but which may also lead to a diagnosis of myocarditis, endocarditis, or pericarditis. Arterial lesions are more commonly met with during convalescence; they occur frequently under the form of arteritis with thrombosis, obliterating the vessel in its entire length (Jiménez and J. Ramírez) and leading to dry gangrene of the lower extremities.

Phlebitis of the lower extremities is met with under the same conditions as arteritis; it may be followed by moist gangrene and sometimes it is the occasion of embolism.

To the dynamic or mechanical disorders of the circulation may be attributed the gangrene of the mouth (noma) observed in children under treatment in the Hospital de San Andrés, and to bedsores on points exposed to pressure, especially over the sacrum, the hips, the elbows, and the heels. The various hemorrhages met with in this disease are to be attributed to like causes, or rather to that condition of the blood which was described above and upon which Jiménez so rightly insists. Epistaxis is not ordinarily very profuse, but it may acquire great importance by reason of its frequent recurrence during the course of the disease, and may even endanger the life of the patient. Hemorrhages from the stomach and intestine have been observed in the course of typhus fever; we shall speak of them again in treating of the differential diagnosis from typhoid fever, and shall also mention those which occur in the meninges.

In the section on pathological anatomy we spoke of the special lesion of the lungs which the French physicians call splenization, and also the induration characteristic of pneumonia which occurs as a complication of typhus fever; this last named should be looked for with great care, since it may occur without any of the usual symptoms, such as pain in the side or prune-juice expectoration. Congestion and œdema of the lungs also occur as complications in this

disease, and the physician should always be on his guard in order to be able to combat them upon their first appearance.

The condition of the kidney should always receive careful attention from the medical attendant. Fortunately involvement of these organs can be early recognized by analysis of the urine.

Termination.

In the previous sections we have said all that is known concerning this point, more especially in the section on symptomatology, apropos of a termination of the disease by the death of the patient. When typhus fever ends in recovery the return to health may be almost instantaneous, or at least the diminution in the gravity of the symptoms occurs with great rapidity. In other cases, however, recovery may take place slowly. I cannot refrain from quoting at some length the words of Jiménez in an article by him, entitled "Tabardillo,"* since they describe so clearly the mode of termination of typhus fever that they will hardly bear condensation. He writes:

"In almost all cases the disease terminates almost suddenly, or at least very rapidly; it is common to encounter a complete change in the condition of the patient between two consecutive visits. The change is announced sometimes by profuse sweating, abundant urination, or a copious discharge from the bowels, giving one the impression of critical phenomena. Very often the patient remains several hours as if asleep or resting; he usually changes from the dorsal decubitus to a position on the side, and upon awakening it is noticed that he takes interest in what is passing about him; he complains of pain and discomfort of which a short time before no evidence was given; the expression of his face is more natural and intelligent; the nostrils and the mouth become moist; the patient is found to have a little appetite, and especially significant is the fact that the pulse becomes slower and regular; in a word, the patient is frankly convalescent, the only symptoms remaining being deafness, some hebetude, torpidity of movement, a certain degree of general hyperæsthesia, and occasionally the petechiæ which disappear gradually in the course of a few days. Inflammation of the parotids and suppurative otitis are, however, rather frequent complications at this period. To speak more exactly, during these moments of transition there arises in various cases a new order of morbid phenomena which are in a measure peculiar to typhus and which, by reason of the great practical importance which they present, oblige me to delay a few moments in this study of the signs of convalescence.

"Among the first sensations that the patient feels upon emerging

from his malady is sometimes an uneasy sensation, almost a pain, in the legs (the most common seat of this symptom), or a more or less acute pain and rigidity of the parts. Upon examination of the legs we find one of two things: 1. Either the legs are warmer than the rest of the body, somewhat swollen and red, and the arteries are felt to pulsate more strongly; these symptoms, to which is joined a recrudescence of the fever, increase rapidly until they give to the limb the appearance of phlegmasia alba dolens. 2. In the other case the limb is more or less insensible and colder, and pulsation in the arteries of the member ceases at once and completely. In this second case the fever also again increases, and spontaneous pains of very variable intensity, accompanied by a feeling of numbness, of formication, or of electric shocks, follow; the coldness of the limb increases; the color, beginning from the toes, passes from red to livid and finally becomes black; the parts become dry and indurated, and crackle like a sheet of paper—in a word, they become mummified. Sometimes a zone of inflammation may arise at the limits of this alteration, resembling the line of demarcation; but it is not always of this salutary character; for it may simply afford to the gangrenous process a new support for the invasion of other portions of the member. While reserving the study of these accidents to another occasion I think that this description will suffice to give an idea of the peculiar and great danger to which a convalescent from typhus fever is exposed."

I ought to add here that in the cases which I have observed personally gangrene has not occurred with the frequency that it would appear from the author just quoted we ought to expect, but it is nevertheless a complication that occasionally occurs.

Diagnosis.

The description which I have given of typhus fever in the opening paragraph of the section on symptomatology demonstrates to my mind that it is a perfectly well-defined disease, different from all others; and while some of its symptoms taken singly might cause confusion with other affections, nevertheless it can be distinguished by the conditions under which it develops, the course which it follows, and its chief symptoms, among them especially the characteristic eruption. However, following the custom established by all medical writers I shall compare the disease with those affections which more closely resemble it, emphasizing the differences between them.

In the first place typhus fever resembles all the grave infectious diseases which in their most acute stage have the same symptomatic

expression, designated by the general term of typhoid or typhous condition, that is to say, stupor, which, as we have before remarked, is the symptom to which the disease under consideration owes its name.

Typhoid Fever.—The disease which most resembles typhus fever and which, for a long period, was confounded with it, is typhoid fever. The two may be differentiated by the following characteristics: In the first place, the constant cause of typhoid fever is Eberth's bacillus, found upon examination of blood taken from the spleen. Up to the present, however, we do not know what microorganism or what toxins are responsible for typhus fever. Typhoid fever is communicated by means of the dejections, either directly or through water which has been contaminated by Eberth's bacillus. This fact, that is to say, the production of typhoid fever through the medium of water, has been perfectly demonstrated by numerous and conclusive observations and also by experiment. Up to the present, however, the conveyance of typhus fever by drinking-water has not been demonstrated. Let us remember that it originates frequently where there are many human beings gathered together: in prisons, in ships, in confined dwellings of the poor, and in military camps, that is to say, where there is a crowding together at the same time that there is an insufficiency of respirable air, scarcity of food, and uncleanliness of clothing and dwellings, or where men have been reduced by hunger, fatigue, and privation. Repeated and conclusive observations have shown that typhus fever is spread by contagion, and therefore, when there is any doubt as to the nature of the disease, we should take into consideration whether or no the patient under observation has been exposed to the contagion of typhus fever.

Typhoid fever is ushered in by prodromes; typhus fever appears suddenly in the majority of cases. In typhoid fever the elevation of temperature is constant from the first; in typhus fever it may be intermittent or remittent in the early days of the disease.

Epistaxis appears at the end of the first week or even later in the course of the disease in typhoid fever; in typhus fever it occurs on the third or fourth day. We must not forget that it may consist in no more than the loss of a few drops of blood. In typhoid fever the exanthem consists of a few rose-colored spots, scattered over the abdomen, chest, and back, and it is very rare to find petechial spots; it appears at the end of the first week. In typhus fever the eruption is perfectly characteristic; it appears on the fifth day of the disease very constantly in my experience, but from the fourth to the sixth day, according to most authors; it appears first on the abdomen, extending thence to the chest, the back, and the upper and lower extremities; it is confluent and may sometimes cover the entire body

with the exception of the face. It is formed of small spots and sometimes of wheals of slight elevation, of a more or less dark pink color, which disappear under pressure of the finger, but immediately reappear when this pressure it removed; the duration of each individual patch is from two to ten days; the color changes gradually to a reddish gray, or more commonly a wine color, and after a while assumes an ecchymotic character, no longer disappearing under pressure; if the patient dies the exanthem may be observed even on the cadaver, if he recovers it may be seen well into convalescence. In spite of assertions to the contrary there may be desquamation following the eruption, instances of which I have myself noted. As may be seen from this comparison, it is impossible to confound the eruption of typhus fever with that of typhoid.

In typhoid fever the headache is severe, in typhus fever it is early, continuous, very intense, and frontal in location; it ceases usually on the eighth day.

Insomnia exists in typhoid fever, but is neither so early in its appearance nor so obstinate as in typhus fever, in which it persists unless overcome by the stupor. Deafness is little marked in typhoid fever, but is pronounced in typhus. Vertigo is less marked in typhoid fever, but is very accentuated in typhus fever, and appears whenever the patient stands on his feet, rises in the bed, raises his head, or even moves it from one side to the other.

The delirium is more characteristic and more precocious in typhus than in typhoid fever; it is ordinarily quiet in character in the former disease, and the patient seems to be talking in a low voice or to himself; in young and robust individuals, in alcoholic subjects, or in the ataxic form of typhus fever the delirium is noisy, agitated, and violent. Stupor, which is occasionally marked even in typhoid fever, is a very characteristic feature in typhus; the face is congested, the conjunctivæ are red, the expression of the eyes is like that of a drunken man, and the patient has a dull air and appears to be uninterested in anything taking place about him. These symptoms are less marked in typhoid fever.

In typhoid fever the muscular pains are less intense as a rule than in typhus fever; the sense of fatigue is less and so also is the loss of strength. In typhus fever the fatigue is more marked, the loss of strength is earlier, and, as a consequence of this, the dorsal decubitus is the rule; in an advanced stage of the disease the muscular resolution is complete.

In typhus fever the nasal mucous membrane is constantly dry and frequently furfuraceous; the mouth is dry, the teeth are covered with sordes; the tongue is dry from the beginning of the disease and

the dryness increases to such an extent that it becomes difficult to extrude the tongue from the mouth, and when it is put out it trembles between the lips. The pharyngeal wall is also dry and covered with mucus.

In typhoid fever the gurgling in the right iliac fossa upon pressure is constant; in typhus fever this symptom is encountered rarely and only when diarrhœa exists. In the latter disease meteorism exists when the bowels have not been regularly evacuated and in the later stages is almost constant, and the same is true of the general tenderness on pressure. In typhoid fever diarrhœa is the rule, in typhus fever constipation. Intestinal hemorrhages are frequent in typhoid fever, but exceptional in typhus.

In typhoid fever ulceration of Peyer's patches is so constant that it is regarded as a characteristic lesion of the disease and has served to give to the affection the name of dothinenteria; in typhus fever there is no ulceration of Peyer's patches; they may occasionally be slightly enlarged, showing numerous black points, compared to a recently shaven chin (Jiménez), but they are not ulcerated. The frequency of intestinal hemorrhage in typhoid fever is explained by the fact of the ulceration of Peyer's patches; and when this process invades all the coats of the intestine it results in perforation with consecutive peritonitis; in typhus fever the fact that there is no ulceration of Peyer's patches explains the absence of hemorrhage, of intestinal perforation, and of consequent peritonitis. I have never seen this last-named condition in a patient with typhus fever. In the rare cases in which intestinal hemorrhage takes place in typhus fever it does not result from ulceration of a vessel as in typhoid fever, but from exudation, such as we see in all grave conditions of the economy.

The peculiar odor observed in patients suffering from typhus fever, which is *sui generis*, is not found in typhoid fever.

The course of the disease in typhoid fever is continuous from the beginning; in typhus fever the symptoms may intermit during the early days and we may observe a remission between the ninth and the eleventh days. In typhoid fever the symptoms become progressively and slowly worse; in typhus fever they develop with great rapidity and by the end of the first week have reached their almost complete development. In typhoid fever the symptoms on the part of the nervous system are less marked than they are in typhus; in the latter they are precocious and prominent, and their symptomatic expression is so constant and so peculiar that they have served to give the name of "cerebral fever" to the disease. In typhoid fever all the symptoms are very clearly marked during the second week, but they do not attain their full development until the third week; in

typhus fever the second week is marked by the aggravation of all the symptoms, and during this week the patients take on the characteristic appearance which has served to give the name to the affection, that is to say, stupor.

Typhoid fever, when it is going to terminate in recovery, subsides very slowly; typhus fever may also decrease very slowly, the defervescence beginning from the ninth to the eleventh day, but it may, on the other hand, decline very rapidly, a fact which has been noted by all writers on the disease. The mean duration of typhoid fever is three weeks, but it may be prolonged for thirty or forty days; that of typhus fever is fourteen days, its extreme limits being the eighth, very rarely, and the twenty-first, more commonly. The convalescence from typhoid fever is slow and tedious; that of typhus fever is more rapid and frank. In typhoid fever phlebitis and arteritis are not common complications or sequelæ; in typhus fever, in Mexico at least, phlebitis is frequently seen, and even more frequently arteritis terminating in gangrene of the extremities.

A comparative study of the symptoms of the two diseases gives us the means of distinguishing them clinically, but if doubt still remains in the mind of the observer he may resort to the serum diagnosis. A French physician, J. Widal, has discovered the existence of an agglutinating reaction in the blood serum of patients with typhoid fever when this is in the presence of cultures of Eberth's bacillus. The way in which this test is made is the following: From the fold of the elbow, the skin being made aseptic, a small quantity of blood is extracted with a syringe, and is mixed with a bouillon culture of the typhoid bacillus in the proportion of 1: 10 (eight drops of serum in 4 c.c. of bouillon), and is placed in the oven at a temperature of 37° C. At the end of twenty-four hours, sometimes earlier, a few flakes are seen at the bottom of the test-tube, and the fluid is rendered turbid by the presence of a whitish powder. It is always well, in order to be sure of this change, to compare the contents of this tube with those of a control tube. The appearance which the fluid assumes is due to the agglutinating power which the serum of a typhoid-fever sufferer possesses in the presence of Eberth's bacilli. Widal[10] has recently modified this procedure, making it more simple and more rapid. To twelve drops of the culture fluid he adds one drop of blood drawn by the prick of a needle, and then examines a drop of this mixture under the microscope, comparing it with a drop of a control mixture. If in this preparation numerous confluent masses of bacilli resembling an archipelago are seen, the diagnosis of typhoid fever is positive. The appearance noted is seen with increasing distinctness from fifteen to thirty minutes after the mixture has been made.

Widal's reaction is also manifested during convalescence from typhoid fever; in the child it lasts for two months, and in the adult it persists for four or five months. In some cases this reaction is not manifested before the end of the first week of the disease and it may also be absent for a few days preceding death. The reaction is a phenomenon of infection and not of immunization.

We have entered into these details in order to differentiate typhus from typhoid fever, because in the two diseases we find in its highest degree the expression of the collection of symptoms, of the syndrome, which has been called the typhoid condition. This typhoid state is a late expression of infectious diseases of whatever origin, and it is because of its presence that many fevers essentially different have been confounded under the one name, and that many distinguished practitioners have even been led into the error of confounding at the bedside the typhoid form of certain diseases such as measles, scarlet fever, and certain forms of apical pneumonia with typhus fever. By reason of the resemblance between typhus and typhoid fever the two affections were not distinguished for a long period. The differential diagnosis has been facilitated also by the observation made by Lombard, of Geneva, in 1836, that the ulcerations of the intestine, such as had been described by Louis of France in typhoid fever, were not met with in the typhus fever of Ireland; by that made in the following year by Dr. Gerhard of Philadelphia, a student of this Louis; and by that which Gerhard made in collaboration with Pennock, that there exists a difference not only in the anatomical characters, but also in the etiology, the symptomatology, and the prognosis. In 1844 a very distinguished Mexican physician, Miguel F. Jiménez undertook a study of the differences existing between typhoid fever, such as described by Louis and Andral, and the similar disease which he had constantly observed in the city of Mexico and which the local physicians had confounded with the affection described by the French authors. Dr. Jiménez made his investigations on more than three hundred personal cases. He described with a master hand under the name of "Tabardillo," the disease which prevailed throughout the central plateau of Anáhuac, and which was the same as that which the North American physicians just mentioned had described a few years before, following Jenner and Murchison of Edinburgh, Flint of Buffalo, Geisinger in Germany, Landouzy, Forget, and Jacquot in France.

Relapsing Fever.—Another disease which has been confounded with typhus fever is recurrent typhus or relapsing fever. This disease is differentiated from typhus fever in the first place by the fact that in the former during the access of the fever the blood of the patient contains certain special organisms described by Obermeier and

known as Obermeier's spirochætæ. This parasite is a delicate mobile spirillum, which is not met with in the blood in any other disease and the occurrence of which distinguishes this disease from typhus fever. Relapsing fever owes its name to the fact that it is characterized by attacks of very intense fever, lasting for from five to seven days and separated by intervals of like duration. The two characteristics mentioned, namely, that of the presence of the spirillum in the blood and the peculiar course of the disease, serve to distinguish it from typhus fever, although it is also differentiated by certain peculiarities in its symptomatology, such as the preservation of the intellectual functions, the absence of the characteristic eruption of typhus fever, and the coëxistence of icterus, which is very frequently met with in relapsing fever; also by the fact that it is less grave and that it terminates speedily in convalescence; and above all by the interval between the pyrexial attacks, lasting for from five to seven days, followed by a new attack of nearly the same duration. I may add also that relapsing fever has never been observed in the republic of Mexico.

Remittent Fever.—That form of remittent fever which is observed in temperate climates can scarcely be confounded with typhus fever, but it is otherwise with the form met with in tropical regions, which has been described under the name of typhoid or malignant remittent fever, or "jungle fever." This form of malarial infection may take on typhoid symptoms just as all the other grave infectious diseases; but in addition to the facts that it develops in marshy regions, that it is not contagious, and that the characteristic eruption of typhus fever is wanting, it may also be differentiated by an analysis of the blood, the plasmodia described by Laveran being found in the blood of malaria; it is also differentiated by the therapeutic action of salts of quinine, which have no effect in typhus fever; and finally, the grave form of malarial infection is not usually observed in localities where typhus fever prevails. In Mexico the grave remittent fevers are met with on the two sea coasts, exactly where typhus fever is not encountered.

Yellow Fever.—This fever in its grave form is marked by typhoid symptoms in consequence of which it might be confounded with typhus fever; but this could only happen in those countries in which yellow fever prevails endemically, or in which it frequently occurs in epidemic form. It may be distinguished, however, from typhus fever, by its shorter duration, by the absence of the characteristic eruption, by the yellow coloration of the skin, by the black vomit, and possibly also by the detection of the bacillus icteroides discovered recently by Sanarelli,[1] of Montevideo, and which has also been

found by other observers. It is to be noted that in the Mexican republic yellow fever is found on the coast line, not above an elevation of 1,000 metres (3,250 feet), while typhus fever occurs in the central plateau lying at least 2,000 metres (6,500 feet) above the level of the sea, and is never found endemically in the zone lying between 1,000 and 2,000 metres of elevation.

Purpura.—This affection can hardly be confounded with typhus fever since it is not accompanied by fever and since the petechiæ (if such a name may be given to the ecchymoses) appear primarily and not late in the course of the eruption; it is also distinguished by the facts that the hemorrhages take place from other than the nasal mucous membranes and that the affection occurs in cachectic individuals and independent of contagion. Indeed, practically, it would be very difficult to confound the two affections.

Measles.—This disease ought not to be confounded with typhus fever for the reason that it occurs ordinarily in childhood, and that it is always preceded by an intense catarrhal inflammation of the conjunctivæ, the nasal fossæ, the larynx, and the bronchial tubes. The two affections may also be differentiated by the fact that the eruption occurs earlier in measles than in typhus fever and differs from the latter in its evolution, and finally, by the epidemic conditions prevailing at the time.

Meningitis and Encephalitis.—These two affections might be confounded with typhus fever because of the cerebral symptoms which are common to all, but there are differences which may be discovered on careful investigation. The cephalalgia is more intense in meningitis, is boring and pulsating in character, and seems as though it would split the head; in typhus fever the headache is frontal, distressing, and continuous. The injection of the eyes in meningitis is less marked than in typhus fever. In meningitis the expression of the eyes is animated, but in typhus fever it is like that of a drunken man. There is no photophobia in typhus fever, but it is very marked in meningitis. While the character of the delirium may in certain cases give rise to error, the presence of the eruption in typhus fever will suffice to distinguish the two affections. The nausea and vomiting which are so common in meningitis are entirely wanting in typhus fever. The course of the two diseases varies, as does also their duration. In typhus fever there is no true inflammation of the meninges or of the brain. In children the hydrocephalic cry is a characteristic symptom which will enable us to make an early differential diagnosis.

Delirium Tremens.—The circumstances under which this delirium develops will suffice to distinguish it from typhus fever; it is not ac-

companied by high fever, the patient presents no eruption such as that characteristic of typhus, and the course and duration of the two affections are different; in a word, there is no resemblance except in the delirium.

Pneumonia.—When this affection assumes the typhoid form it may resemble typhus fever; this is especially the case in the latent form attacking the apices and occurring chiefly in the aged. If an examination of the chest reveals the presence of the pathognomonic signs of pneumonia, then the typhoid state should be regarded as a complication of this disease. But if the symptoms proper to pneumonia only become manifest several days after the existence of the febrile state the pneumonia must be regarded as a complication of typhus fever, especially when the characteristic eruption of the latter disease is present.

Uræmia.—The typhoid form of this intoxication may be confounded with typhus fever; like the latter it is the symptomatic expression of an infection, but it may be differentiated by the absence of fever, by the previous occurrence of symptoms of nephritis, and occasionally by the presence at the time of examination of traces of gouty antecedents; in a word, a comparison of the characteristic symptoms of the two diseases will suffice to prevent error in diagnosis.

We cannot mention all the other diseases which may at times assume the typhoid state since they are so very numerous, and moreover their differentiation is usually without difficulty. There are two, however, concerning which a word must be said, namely, grave intestinal infection (stercoræmia) and retained placenta. The differentiation of typhus fever from stercoræmia is based chiefly upon the rapid and favorable results of purgative medication. In the case of retention of the placenta, doubt may arise on account of the long interval which may have elapsed since parturition, sometimes as much as twenty days; but a careful exploration followed by extraction of the placental remains will clear up the diagnosis.

To sum up: Typhus fever has a special aspect of its own, it is a well-characterized morbid entity; it is a perfectly well-defined species in the family of infectious continued fevers; its prominent characters are the suddenness of invasion, the date of the appearance of the epistaxis and of the eruption, the aspect of the latter, the insomnia, the cephalalgia, the precocity and intensity of all the other cerebral symptoms, its cyclic march, its average duration of fourteen days, and the absence of intestinal lesions.

Prognosis.

In determining the prognosis of typhus fever the first idea that occurs to one is to ascertain the proportion of deaths among those attacked by the disease. If, however, we have recourse to statistics we find such differences in the motality figures that we are forced to the conclusion that the conditions existent in the various epidemics which have furnished the basis of these statistics must have differed greatly. In the first place it is evident that the mortality of typhus fever prevailing endemically in a certain locality must differ from that of the same disease during an epidemic outbreak; the number of victims of the endemic form varies according to the seasons, and furthermore the mortality of an ordinary epidemic outbreak will not be the same as that of an epidemic which arises under conditions of famine or widespread misery or which is favored by war. As we have said in the section on the history of the disease, the great armies spread typhus fever throughout Europe, and the ravages which the disease caused were in proportion to the distress which the war had brought in its train. We cannot compare the mortality from typhus fever in rural districts, where the people live for the most part in the open air, with that in besieged cities, where the inhabitants are crowded together, food is scarce, and the morale of the population is depressed by privation and by terror. Similar untoward conditions exist in ships making long voyages or detained by calms, in prisons were the hygiene is of the poorest, and formerly in the galleys. These considerations have led us to study the gravity of typhus fever in relation to age and sex, to the previous condition of health or disease, to the habits of sobriety or intemperance, and to all the other conditions which may influence the organism in the direction of a lessened resisting-power against the germs of the disease. This way appears to us to be the best in a work which aims to give to the practising physician the grounds upon which to base his prognosis, not in a general sense but as regards the individual patient.

Age.—From the tables constructed by Murchison from the data furnished by the records of the London Fever Hospital from 1847 to 1870, it appears that the mortality of typhus fever is less in the young than in adults, and less in adults than in the aged. The relative mortality for each period of five years was as follows: During the first five years it was 6.60 per cent., in the period from five to ten years it fell to 3.59, beween ten and fifteen years it fell still further to 2.28, but in the next period of five years it rose to 4.46 per cent. Thus we see that the mortality decreases from the first to

the third lustrum, but begins to increase in the fourth. From that age upwards the increase is very rapid, as we may see in the following table from Murchison:

From	30	to	40	years	the mortality was	35.39	per cent.
"	40	"	50	"	"	43.48	"
"	50	"	60	"	"	53.87	"
Above			60	"	"	67.04	"

The data collected in the city of Mexico by the Superior Council of Health confirm in a general way the figures of Murchison, as is shown in the following table, which embraces the period from August, 1891, to December, 1897:

Ages.	Deaths.			Percentage of the total deaths.
	Males.	Females.	Total.	
From 0 to 1 year	4	6	10	0.16
" 1 " 2 years	4	11	15	0.24
" 2 " 5 "	31	27	58	0.93
" 5 " 10 "	54	72	126	2.02
" 10 " 20 "	387	330	717	11.52
" 20 " 30 "	1,154	786	1,940	31.17
" 30 " 50 "	1,466	1,146	2,612	41.97
" 50 " 70 "	335	358	693	11.13
" 70 " 90 "	22	30	52	0.83
Totals	3,457	2,766	6,223	

We find from this table, representing a total of 6,223 deaths from typhus fever, a confirmation of the statement that the mortality increases with the age, very slightly up to the age of ten years, but rapidly from ten to twenty years; that it is almost three times greater from twenty to thirty than from ten to twenty; that the percentage of deaths from typhus fever, as compared with the general death-rate, is highest between the ages of thirty and fifty years; and that it diminishes from fifty to seventy years, and very markedly in the period between seventy and ninety years. These figures do not seem to be in accord with those of Murchison, but the contradiction is found to be less apparent when we consider that the number of those attacked from fifty years upwards is less, and that the number of inhabitants between seventy and ninety years of age is very small in Mexico.

Sex.—From Murchison's tables we find that the general mortality in the London Fever Hospital during twenty-three years was 19.67 per cent. males and 18.20 per cent. females. From the data collected by Terrés, in the memoir above mentioned, we find that in the different cities of Mexico, out of a total of 6,042 deaths from typhus fever,

there were 3,226 of the male sex and 2,816 of the female. According to the figures of the Superior Council of Health, as shown in the table above, in a total of 6,223 there were 3,457 of the male sex and 2,766 of the female. Thus we see that the mortality is greater among men than among women.

From a study of his own cases and others collected from various sources, Murchison concludes that the disease is, at any given age, more grave in men than in women, and he adds that in man not only is there a more active organic disintegration under the influence of the pyrexia, but probably also the habits of intemperance and other circumstances tend to affect the liver and the kidneys, thus rendering elimination more difficult.

Social Position.—In order to judge of the varying gravity of typhus fever according to the differences in social position, Murchison divided the patients treated in the London Fever Hospital during a period of fourteen years into three classes, viz.: (1) pay patients; (2) patients admitted free, yet not classed as paupers; and (3) paupers. His results were as follows: In the first class the mortality was 14.89 per cent., in the second it was 18.58, and in the third class 27.64. He attributed the increase of mortality observed among the poorer class to the greater age of these patients. He says that in Ireland the general belief is that typhus fever is more grave in its results among the rich than among the poor. Of more importance than the financial condition of the patients, as regards the gravity of typhus fever, is the amount of cerebral labor performed, and this work is greater among the educated classes than among the poor and ignorant.

Previous Condition of Health and Intemperance.—Alcoholism, which produces disease in the heart and arterial system and in the nervous centres, places the individuals attacked by typhus fever under more unfavorable conditions than are those of the same age and the same sex whose habits are temperate, since, as we have seen above, the circulatory and nervous systems suffer greatly in typhus fever. Statistics bear out this assertion. When there is a history of gout and rheumatism the prognosis is much worse, and the same may be said in regard to hepatic and renal disorders. We may derive information of value in forming a prognosis from examination of the urine. Señor J. D. Morales, Professor of Pharmacy in the University of Mexico, has reached the conclusion, from a study of the analyses of urine in two hundred cases of typhus fever, that the diminished quantity of urine excreted is in direct relation with the gravity of the disase, and he regards anuria as a symptom of fatal import. The urine is turbid in typhus fever (usually), but if it is

transparent and this transparency is preserved into the second week it is to be regarded as a favorable prognostic sign. If hyaline casts are found, and especially pigmentary granulations, from the fifth day of the disease, and if they are present for a period of three days, Señor Morales says that death will result. A rise in the specific gravity to 1.033 is of grave significance. If albumin is present in a proportion of more than half a gram per litre it is a sign of the greatest gravity. Of equal gravity is hæmoglobinuria or hæmaturia, provided always that this is not due to the presence of menstrual blood. Finally, he regards the presence of urobilin and of the biliary pigments and acids as an unfavorable sign when they are present in large amount, and peptonuria is also of evil import.

All those diseases which weaken the organism render it less able to contend successfully against the disorders which an infection as grave as is typhus fever produces in most of the organs, and therefore by their presence they render the prognosis more serious.

Observation has shown that there is a certain conjunction of circumstances in which an unfavorable termination of the disease is to be feared. These are "the advanced age of the patient, the epidemic presence of the disease, the rapid occurrence of the characteristic facies, great intensity of the headache, furious character of the delirium, profound stupor almost reaching coma, carphologia, hiccough, frequency and profusion of epistaxis, confluence of the eruption with very large patches of a dusky hue, gangrenous appearance of the skin where pressure occurs or where there are blisters, the occurrence of vesication, a dried and shrunken aspect of the skin, retention of urine, involuntary evacuations of liquid and foul-smelling stools, the complication by pneumonia, any irregularity in the development of the symptoms, and an exaggerated rapidity of the pulse. In regard to this last-mentioned symptom we may remark that in the majority of cases the pulse is 108 to 120 a minute; in some cases, when the disease is of very benign appearance, the pulse may be only 100 or a little over during the first few days, but it becomes more rapid as time goes on, and if the rapidity is now accompanied by irregularity or other evidences of a more or less severe alteration the patient will succumb" (Jiménez). I may add from my own experience that the occurrence (early) of a disproportion between the pulse rate and temperature is a sign of fatal omen.

On the other hand, we are to regard as favorable factors "the youth of the patient up to fifteen years, the preservation of the mental faculties and the strength, the appreciation by the patient of his own needs, tranquil sleep, moisture of the nasal fossæ, moist heat of the skin, moisture of the mouth and absence of sordes, regularity in the

excretions, regularity and moderate frequency of the pulse, and the normal progression of all the symptoms" (Jiménez).

These two groupings of the symptoms will be of great assistance in forming a definite prognosis. Nevertheless, all observers are agreed that typhus fever of apparently benign course may terminate in death, especially in the aged; and, on the other hand, a case of typhus fever of seemingly great gravity may result in recovery.

Prophylaxis.

It is usual to include the subject of prophylaxis in the first part of the section on treatment of a disease. This is correct when we are treating of smallpox or rabies, for which diseases we have preventive measures of incontestable and practical efficacy, such as the vaccination of Jenner and the preventive inoculations of Pasteur. We doubt not that in the future a vaccine against typhus fever will be discovered, but we have none as yet. In the mean while we must perforce limit our preventive measures to shutting off communication between those sick with typhus fever and the well.

Isolation of the patient and disinfection of his dejections, of his underclothing, and of objects which have been in mediate or immediate contact with him, such as the clothing of his attendants, the furniture, the room in which he has been, etc., are the means by which we prevent communication of typhus fever to those in the neighborhood of the patient. Isolation can always be more effectively carried out in special hospitals, where the authorities may employ suitable measures which cannot be instituted in civil practice. In order that the isolation may be efficacious it is necessary to enforce it as rigorously as possible; it is necessary that not only the patient, but his attendants as well, should be strictly isolated. The manner in which isolation of cholera patients arriving at English ports is carried out, as well as the way in which those suffering from the same disease who arrived in New York from Hamburg in 1892 were isolated, will serve as a model. It would be well if these practices were adopted by the public authorities in all countries as regards typhus fever and other infectious diseases of the same nature.

When the patients cannot be carried to a hospital they must be isolated in their own homes, in well-ventilated rooms from which all hangings and carpets have been removed and in which only the absolutely necessary furniture has been left. The attendants should be selected from among those who have already had typhus fever, since it is known that one attack of this disease confers immunity (usually). It is to be recommended that the nurses or other attendants should

not sleep in the same room or take their meals there; that before eating they should wash hands and mouth with suitable disinfectants; that they should not communicate with the other members of the family in any manner whatever, if this is possible, or, if it is not, that the communication should be as limited and as guarded as the circumstances will permit. The dejections should be received in vessels containing disinfectant solutions, and the underclothing should be immersed in a similar solution before being sent to the laundry.

When we shall have discovered the germ which is the cause of typhus fever the number of precautions which we have indicated will be greatly reduced, as it is even now in the case of cholera and of tuberculosis, the pathogenic microorganisms of which affections have been well studied; but the precautions which we now recommend, empirical as they are, have enabled us to prevent the communication of typhus fever from the ill to the well. As we said in the section on etiology, in Mexico typhus fever is not spread when the rules above indicated are observed, when the clothing of the patients is frequently changed, and when they themselves are treated in the manner which we shall indicate in the following section.

Disinfection is complementary to isolation. It is carried out in the case of the dejections, not because it has yet been proved that these may serve as a vehicle of contagion, but simply as a measure of precaution. We insure the disinfection of the bedclothes and underclothing of the patients in the hot-air oven, that of the furniture and dwellings by means of bichloride of mercury solution, that of objects which might be injured by this by means of a five-per-cent. solution of carbolic acid, and that of delicate bric-a-brac, fine textures, or objects of art which, through inadvertence, or any other reason, have been left in the sick-room, by means of formic aldehyde. It is possible that these precautions are more than is necessary, but that is because we are yet ignorant of the germ of contagion and its means of transport. A simplification in the methods will come later.

Although this is not the place to dwell in detail on measures relative to public hygiene and which we cannot doubt will prevent the disease from spreading throughout a city, we may, nevertheless, recall that, while treating of the causes of typhus fever, we related certain facts proving the influence which fecal emanations have in the production of typhus fever, and showed from this the necessity for the removal of all such matters from the interior of dwellings beyond the outskirts of the city by means of impermeable conduits having a sufficient fall and thoroughly flushed by a continuous stream of water. The proper location of water-closets and of all the drains inside houses also comes within the domain of hygiene. This

recalls also all the other works of public sanitation recommended by hygienists and which probably will succeed some day in causing the disappearance of typhus fever from civilized communities.

Another measure which experience has proved to be efficacious in preventing the spread of typhus fever is the removal from populous centres of the crowds of beggars and tramps. Dr. Jesús E. Monjáres, of San Luis Potosí, has informed me that in this city the removal of the crowds of beggars who swarmed its streets sufficed to cause the disappearance of an epidemic of typhus fever which was prevailing there. Brouardel, in the work above cited, confirms this view and declares that all vagabonds should be regarded as suspects, and that they should not be received into hospitals, asylums, or prisons without having previously been subjected to precautionary measures; their clothing should be removed, their hair should be cut, and they should be made to take a bath, being then given clean clothes furnished by the establishment, those which they had previously worn being disinfected.

In Mexico the clothing of all patients brought to the typhus-fever hospital is disinfected and is returned to the patients upon leaving the hospital after they have taken a bath.

Treatment.

Up to the present we know of no specific remedy for the cure of typhus fever. The report upon the treatment of diphtheria by the serums of Behring and Roux presented to the International Medical Congress in 1897 has removed all doubts as to the utility of this curative measure and has awakened a hope that a similar method of cure may be discovered in the case of typhus fever.

Orrhotherapy.—The attempts made in Europe and America to treat virulent diseases by means of the blood serum of animals which are naturally immune, or which have been rendered immune artificially, suggested to me the idea of using as a curative remedy in typhus fever the blood serum of convalescents from this disease. We know that one attack of typhus fever as a general rule confers immunity upon the person who has suffered from it. Although this immunity is not absolute, as the rare instances of repeated attacks of typhus fever would indicate (see above in the section on etiology), it may, nevertheless, be assumed that one who is only convalescent from the disease, or who has had it but a short time before, has acquired at least temporarily absolute immunity. Starting from these considerations I sought among the convalescents from typhus fever those who were young and who had been in good health prior to the attack from

which they were emerging, those who had had no diathetic troubles previously, and in whom the convalescence was frank. I obtained from these, using the strictest aseptic precautions, a small quantity of blood drawn directly from the veins into sterilized tubes.

The first patient in whom I employed this method of treatment was a young man of twenty years, previously healthy and robust, in whom it was to be expected that the disease would follow a typical course. I began injections of blood serum from a typhus-fever convalescent on the seventh day, in doses of 3 c.c., increased in the following days to 4, 5, 6, 8, and 12 c.c. The disease terminated on the fourteenth day, so that it was not cut short; neither was the delirium affected, for it persisted even one day after the temperature had dropped to normal. In other cases in which I employed the same remedy in larger doses I was unable to convince myself that the serum exerted a favorable influence on the duration of the disease, but neither could I see that it had any injurious effect upon the patient. I have been unable to continue my observations for the reason that during these past two years, the endemic of typhus fever has been at a minimum in the city of Mexico (from seven to ten deaths a week in a population of 350,000), and I have not now at my disposal any special service of typhus-fever patients. I think, however, that the subject is well worthy of further investigation.

Dr. Nicolás Ramírez de Arellano and Dr. Ismael Prieto, the first named a member of the Superior Council of Health and the second the Chief of the Bacteriological Laboratory of this same Council, have suggested a similar therapeutic procedure. These gentlemen believe with me that the blood serum of convalescents from typhus fever is endowed with curative properties against this disease; but they propose in order to practise the orrhotherapy of typhus to follow the methods that other authors have employed for the cure of other transmissible diseases. The usual procedure consists in injecting into an animal endowed with natural immunity fluids or tissues which contain the specific agent, in withdrawing the blood after the animal has received a series of injections, and in then injecting the serum of this blood into the patient. So their plan is to inject the blood of typhus-fever patients into certain animals and, after a series of such injections have been made, to extract the serum from the blood of these animals and employ it therapeutically for the cure of typhus fever in man.

Another member of the Council of Health, Professor of Veterinary Medicine José L. Gómez, injects into the horse cultures of the microbe of which we spoke in the section on etiology, and after a variable number of injections takes the serum from the blood of this

horse and inoculates with it those ill of typhus fever. His observations have up to the present been very few, and we are unable to draw from them any definite conclusion; it has been demonstrated, however, that they are innocuous.

As we see, therefore, some attempts in the way of orrhotherapy have been made, but have given as yet no practical results. Even if a curative measure were found, we could not hope that it would have any action upon the lesions already present in the tissues at the time the treatment was begun. Yet we should persevere in this study, taking advantage of the facts thus far ascertained.

Typhus fever is one of those diseases in which very many alleged specific measures or remedies have been recommended. In this disease more than in any other we have seen the treatment change according to the ideas prevailing as to the nature of the malady and according to the hypotheses formulated in regard to the action of certain medicaments. History has passed judgment upon the uselessness and even injuriousness of certain methods, such as venesection, which have now been definitively proscribed.

At the present time with our notions, however imperfect they may be, concerning bacteria and toxins and their mode of acting upon the organism in infectious diseases, certain rules have been proposed for our therapeutic guidance in the various periods of invasion of the organism by the microbes, of their diffusion through it, of the production of their injurious effects, and of their expulsion. But as we do not know what germ produces typhus fever we cannot know at what moment it enters the organism, how it diffuses itself in it, or how it is eliminated or destroyed. Such a scheme of treatment, which has not yet received the sanction of experience, cannot find place in a treatise of the nature of that which we are writing at the present moment, for the work of which it forms a part has a different aim, namely, to offer to practising physicians only the results of observation and of experience, devoid of all theoretical consideration.

With this end in view let us establish the foundations upon which to base the treatment of typhus fever. Typhus fever is an infection of cyclic course which, when once it has started, ends only in recovery or death and cannot be cut short, as the laity believe and as was formerly believed by physicians themselves. It is true that a practising physician, an excellent observer, and a distinguished clinician, Dr. Graves of Dublin, affirmed that if a dose of tartar emetic be given within the first twenty-four hours of a febrile affection, occurring in one who had been exposed to the contagion of typhus, it is possible to abort it; and this author states that he has seen the disease dis-

appear in the case of physicians and nurses who, being surrounded by typhus-fever patients, had had an intense chill, followed by fever, severe headache, and the other symptoms which typhus fever may present in the first day after its onset. Graves explains in his work the mode of action of this remedy in such conditions, and he is convinced of its efficacy and advises its use whenever a patient is seen under the conditions described by him. Apart from these circumstances, and especially when the disease is already established, it is necessary to remember that any plan which may be offered for the treatment of the affection cannot have for its object the arrest of the progress of the fever, for such an attempt is useless. It is necessary not to forget that the appearance under which typhus fever reveals itself to us is nothing more than the expression of the contest which is established between the vital forces of the organism and the germ which is seeking to gain possession of it, and later the struggle to destroy or expel the germ when it has already invaded the organism; and that this struggle is carried out according to biological laws and that to disturb it inconsiderately is to oppose nature in the work which she has in hand.

While we do not know of any specific remedy, the province of the physician is to aid the organism in its defence against infection, to moderate the symptoms which by their intensity may jeopardize life, to sustain by means of food and proper medication the strength of the individual, and, finally, to place the patient under such hygienic conditions as will help him to emerge victor from the contest.

In accordance with this programme the problem which the physician has to solve is very well defined. In those cases in which the disease follows a regular course, when no symptom assumes a specially grave character, when the forces of the patient are well maintained, when no function of the organism is very greatly disturbed, especially if the patient is young and has previously been in good health, and when the endemic or the epidemic has not taken on a grave character in other patients attacked at the same time—in a word, when the disease is benign, it will suffice to prescribe the remedies which we shall mention below, in order to guide the patient to recovery.

If the case is one occurring in private practice it is necessary to isolate the patient, as we said above in speaking of prophylaxis, in a room of sufficient size, always kept clean and well ventilated, from which the carpets, upholstered furniture, pictures, objects of art, etc., have been removed and in which only the indispensable articles of furniture (among which we include a second cot) remain. It should be remembered that the ventilation sufficient for renewing the air in

the apartment need not be carried so far as to leave all doors open in cold or damp weather, as many persons have inconsiderately advised.

The underclothing and bed clothing should be renewed as frequently as the condition of the patient will permit. The teeth and the mouth of the patient should be cleaned with slightly alkaline solutions or with a solution of borax, especially before any food is taken. During the first few days of the disease the patient himself may perform these ablutions, but when he has lost consciousness of his own acts the nurse must attend to them. By means of a pair of forceps the nurse should introduce a pledget of cotton, soaked in the solution to be used, as far as the posterior wall of the pharynx, sweeping, so to speak, the palate, the tongue, the interior of the cheeks, and the dental arches. Then she should moisten the mucous membranes, including those of the nose, the pharynx, and the buccal cavity, with sterilized glycerin. In the case of female patients it is necessary to observe the same measures of cleanliness in the vagina and vulva, especially if menstruation occurs during the course of the illness. Before going further we would insist upon one point, namely, that typhus-fever patients should be cared for by special nurses who have already had the disease and are therefore presumably immune, and not by members of the family who, on account of their close relationship and the affection which they bear for the patient, will be apt to be wanting in the necessary calmness, and especially since they have not received proper education in the duties of such an occupation which, like all others, requires special knowledge. Dr. Graves always refused to take charge of a case of severe typhus fever unless the nursing was done by a person of special and wide experience. Cleanliness is indispensable, for it is to be remembered that the bad odor which the patient gives off depends not only upon the severity of the disease but also upon the lack of cleanliness of the sufferer himself.

In the benign cases which we are now considering it will suffice to sponge off the whole body once a day with lukewarm water containing alcohol or vinegar, with Florida water, or with a thymol solution. When the temperature is very high and the skin is dry and burning hot, this sponging should be repeated many times a day, for it affords great comfort to the patient.

The *diet* requires special attention on the part of the physician. During the time when it was supposed that visceral inflammation existed in typhus fever, and when consequently an antiphlogistic method of treatment was employed, the patients were submitted to a very strict diet, while at a later period they were overfed. Experience has shown that the first extreme was full of danger to the patient,

while prudence has modified the second. In the first few days of the disease alimentation may be very slight, since, as in all febrile affections, the appetite is lost and digestion is impaired; but at a later period it is necessary to give the patient milk, gruel, or broth at more or less frequent intervals, according to the condition of digestion and according to the amount taken at each time; but the intervals should not be less than three hours and should be still longer during the night, in order that sleep may not be disturbed. We need not insist upon the variations in the diet according to the customs of each country, to the habits of each patient, to the condition of vigor or debility of the individual, and to the depression of his strength caused by the disease. We should insist, however, upon the use of milk, since it is a complete food, of easy digestion, and is absorbed without leaving much residue, because it possesses a marked diuretic action, and also because, according to the investigations of Gilbert and Dominici,[12] it diminishes in a remarkable measure the number of bacteria in the digestive tube. The skill necessary for a proper regulation of the diet in each individual case, as in all other matters, is obtained much better by personal experience than by any written rules; but in any case it is necessary not to forget that the alimentation is intended to repair losses and to supply to each tissue the elements necessary to its life.

The concentration of the fluids in the organism in all cases of grave infection, especially in febrile cases, brings with it thirst as an expression of the necessity of supplying the water which is lost. This necessity is met in many ways which have varied with the ideas concerning the nature of the disease that have prevailed at different periods, but the supply of fluids in some way is indispensable. For example, slightly acidulated beverages have been employed in cases of high fever of inflammatory form; tonic beverages, with wine or a mineral or vegetable acid, when there is much debility or a tendency to hemorrhage, or when the eruption has assumed a markedly petechial aspect; aromatics in cases in which the meteorism has not been lessened by evacuation of the bowels; fluids containing quinine with alcohol in the case of those suffering from the adynamic form of the disease.

As we have already said, *constipation* is frequent in typhus fever and it is necessary to overcome it by means of enemata, which may be medicated if deemed advisable. If these do not suffice we must have recourse to mild laxatives. The systematic administration of purgatives has been recommended by some distinguished practitioners, Dr. Jiménez among the number. Bouchard [13] explains the good effects of purgatives by saying that they cause the expulsion from the

digestive tube not only of the bacteria which are ordinarily found there, but also of the toxins which they secrete, and that thus they contribute to a lightening of the labors of the organs charged with the destruction of these products. In other countries and at former periods drastic purgatives were employed, but this practice has now been universally abandoned. The constant indication in all cases, however, whatever may be the form which the disease has assumed, is to keep the bowels open. Emetics are not indicated except at the beginning of the disease and in cases in which gastric catarrh is well marked. I may mention, however, that Graves recommended tartar emetic in certain forms of delirium.

The *meteorism* which comes on during the second week calls for the administration of remedies increasing intestinal contractility. Turpentine may meet this indication which is, however, ordinarily fulfilled by the remedies given to overcome the constipation.

We have said that *paralysis of the bladder* is a frequent symptom, and the consequent distention may become so great that the action of the sphincter is overcome and there is a dribbling away of the urine. In these cases it is sometimes supposed that there is incontinence of urine, but the truth is that the bladder is full and that the urine which escapes is merely the overflow. The physician should not allow this condition to arise. If he makes a daily exploration of the hypogastrium he will be able to recognize when paralysis of the bladder occurs and will take care to evacuate the viscus by the regular use of a soft catheter under the strictest aseptic precautions. The catheter should be passed every five or six hours, according to the necessities of the case. The urine thus obtained should be analyzed daily to determine whether it is excreted in sufficient amount, whether the quantity of urea is that ordinarily found in cases of pyrexia, whether albumin is present, and if so, in what proportion, and finally, the quantity and character of the mineral constituents. The results of this analysis will enable us to determine the state of nutrition of the patient and the condition of the kidneys, from which we may obtain data of value in prognosis and treatment.

We may stimulate the *renal secretion*, strengthen the heart, and increase arterial tension by means of milk diet, caffeine, in doses of 0.25 to 1 gm. (gr. iv.–xv.), tincture of strophanthus, in doses of five or six drops three or four times a day, or sulphate of sparteine in daily doses of 0.15 to 0.2 gm. (gr. ii.–iii.). Digitalis is a remedy which has been recommended at various times and by many writers to fulfil this indication, but we shall study this medicament when we come to treat of the alterations on the part of the circulatory apparatus.

Headache is a very distressing symptom of the disease and is

treated in various ways: by means of the solution of acetate of ammonia, in doses of a teaspoonful every two or three hours, or of bromide of sodium in doses of 1 to 3 gm. (gr. xv.–xlv.); by the application of cold compresses to the forehead; by enemata of valerianate of ammonia, by evacuation of the bowels, if this has not been previously effected, and by the reduction of the light in the sick-room. In cases of very intense cephalalgia some relief may often be obtained by means of cold affusions to the head, frequently repeated.

Insomnia demands special attention, not only because it distresses the patient, but also because it is liable to prejudice the result of the illness by giving no rest to the cerebral activity. The measures which we have just mentioned in treating of headache may serve to combat the insomnia. Among these measures are the insuring of quiet to the patient, reducing the light admitted to the sick-room, and sponging the skin and changing the clothing at the time for going to sleep; this is also a good time to change the patient's bed and transfer him to one in which the sheets are fresh and the pillow cool and soft. A full tepid bath, if it is not contraindicated by some affection of the respiratory organs, will also be useful. Among the medicinal measures we may resort in the first place to the use of the bromides; I prefer the sodium salt, in order to avoid the dangerous action which the salts of potassium exercise upon the heart, and employ it in doses of 1 gm. (gr. xv.) repeated two or three times during the night. Chloral is a very efficacious remedy. It may be given in doses of half a gram every half-hour until 2 gm. (gr. xxx.) have been taken in syrup by the mouth or by enema. We must, however, not forget the unfavorable effect which this, like all hypnotics, exerts upon the cardiac contractions. We may employ hypnol and urethan in like doses, or even sulphonal, watching the effects of the latter carefully, since I have several times seen it cause intermittency in the pulse. The English physicians use opium by preference, administered by the mouth or by enema. Murchison, however, looks upon it as contraindicated in cases in which the function of the kidneys is disturbed. Graves says that in these conditions the opium may be replaced by belladonna or hyoscyamus, both of which possess the advantage of stimulating the heart and of influencing indirectly the renal functions. Mexican physicians, in general, do not give opium to produce sleep, fearing to increase the constipation.

Delirium.—The measures of which we have spoken above help to moderate the delirium, but if they are not effective we may increase the dose of bromide, giving it in conjunction with preparations of valerian, especially valerianate of ammonia. Musk and camphor do

not produce such a marked effect in delirium as they do in stupor (see below). Prolonged tepid baths and cold affusions or an ice bag to the head are efficacious means when the delirium is intense in young and vigorous persons and when there is no contraindication on the part of the respiratory organs. If the temperature is very high, the skin hot and dry, and the delirium intense, we may resort to the wet pack, applied in the following way: A sheet is wrung out of very cold water and is laid over a rubber sheet previously spread on the bed; on this the patient is placed naked, and he is then rolled up in the sheet and well covered with blankets, so as to excite perspiration. This is a measure which has been found to be exceedingly efficacious in suitable cases. In those cases in which the ordinary symptoms of cerebral excitement are conjoined with subsultus tendinum, Graves' plan was to give the following mixture:

℞ Tartar emetic,	0.05 (gr. ¾)
Camphor,	0.25 (gr. iiiss.)
Musk,	0.50 (gr. vij.)
Laudanum,	10 drops.

Two or three doses of this mixture was usually sufficient to cause sleep from which the patient awakened tranquil.

Stupor.—This, which is the chief symptom of typhus fever, endangers the life of the patient when it is very intense, and is a grave symptom in all cases. As it occurs in all the grave infections it is probable that it is caused by changes in the blood circulating within the brain, which is charged with toxic principles resulting from autointoxication or introduced into the system in the secretions of the pathogenic bacteria. From this manner of regarding the cause of stupor which we observe clinically is derived the method of treatment which we ought to follow. We must favor the elimination of these products by the skin, by the intestine, and above all by the kidney, stimulate the action of the heart, and arouse the nervous system by counter-irritation of the skin and by the administration of diffusible stimulants. This programme may be realized by inducing perspiration, by means of the well-known diaphoretic remedies, by administering hot whiskey and water, covering up the body warmly, and giving acetate or valerianate of ammonia. Purgatives serve in this case not only to empty the bowels and thus accelerate the cerebral circulation, but they also relieve the kidneys of part of their work, since, as Bouchard says, when intestinal antisepsis is effected the urine contains a smaller amount of toxic substances. In this case purgatives are clearly indicated, and it is probable that it was their good effects under such circumstances which led a large number of physicians to adopt the evacuant system as a general mode of treat-

ment of typhus fever. The renal function is increased, as we have already said, by increasing and even exaggerating the quantity of ingested fluid, by making revulsion to the lumbar region, by the administration of digitalis in infusion or powder, or of caffeine in doses of 0.25 gm. (gr. iiiss.) three or four times a day, or, better, by subcutaneous injection of citrate of caffeine dissolved in a benzoate of sodium solution, or by giving this mixture by the mouth; tincture of strophanthus in doses of five drops three or four times a day, or sugar of milk administered in food or drink, in the proportion of 25 to 75 gm. (℥ vi.–xviii.) a day. In a word, all the circulatory stimulants contribute indirectly to increase the quantity of urine.

The kidney is the emunctory through which the organism frees itself from substances which are poisoning it. We cannot resist the impulse to quote once more from the treatise of Bouchard.[13] He says: "We ought then to stimulate the renal function in all febrile diseases which are accompanied by oliguria; this oliguria results frequently from increased perspiration, from an increased pulmonary evaporation in consequence of the febrile tachypnœa, from the diarrhœa, and from the diminution of the ingesta. It is necessary to restore the water withdrawn in excessive amount from the system through these divers emunctories, with detriment to the kidneys. By favoring diuresis we bring about an antisepsis indirectly, expelling from the organism the vital products of the microbes. The urine, which most certainly is the vehicle for the elimination of the physiological poisons produced by the cells, also removes the poisons fabricated in our tissues by pathogenic agents. The urine which eliminates so many poisons is also the vehicle by which the poisons of disease are removed from the system. We ought to stimulate the secretory activity of the kidneys just as much as to contend against the toxic accidents of the infectious diseases." We ought, therefore, to favor the action of the kidneys by every means in our power.

The remedies of which we spoke above which stimulate the nervous system, such as musk and camphor, are indicated here. Barrallier has employed the essential oil of valerian in cases in which the stupor had reached the degree of actual coma, with a really astonishing success, since he obtained one hundred and thirty-five favorable results in one hundred and seventy-two cases, some of them, in the opinion of those who were observing his patients, being nothing short of resurrections. In Mexico we have obtained very notable results, in similar cases, by the administration of asafœtida by enema. Coffee and tea administered in hot infusion are powerful remedies which are daily resorted to with success in practice, and which have given good results in the hands of the English physicians.

Cutaneous revulsion by means of blisters applied to the calves of the legs had a vogue for a considerable period, but the frequency with which ulceration or gangrene followed these blisters led to their abandonment; revulsion to the scalp which has been previously shaved is, however, still resorted to by some authorities. Stimulation of the skin may be made by means of the lotions mentioned at the beginning of this section as of service in cleansing the skin, refreshing it, and stimulating it in a mild degree; if we employ very strong solutions of thymol or vinegar, or pure Florida water, Cologne water, or tincture of musk we may produce quite a sharp irritation of the skin.

Adynamia is not a symptom of the disease; it is rather a special form of typhus fever resulting from the changes produced in the organism by its own toxic elements or by those which are secreted by the pathogenic germs of the disease. The adynamic is a frequent form of typhus fever in persons debilitated by previous disease, by age, by overwork, or by privation; but it may also present itself in association with the ataxic form in young and robust individuals, as we have previously said. It is necessary to guard against it from the very beginning by means of suitable food, the breathing of pure air, a proper regard for the performance of the functions of all the organs, and a diminution of the results of infection through the measures of which we have spoken above; but there are also certain remedies which are especially indicated here, such as the tonics, and especially cinchona and its alkaloids. It is necessary to stimulate the action of the vasomotor nerves by means of strychnine. It is a frequent practice of Mexican physicians to give hypodermic injections of sulphate of strychnine as soon as the loss of strength begins to be apparent, and to continue them throughout the entire course of the disease, increasing the dose gradually from 2 mgm. to 8, 10, or 12 mgm. (gr. $\frac{1}{30}$ – $\frac{1}{6}$) per diem.

This is the proper place to speak of the use of *alcoholic stimulants*, which have been systematically employed in the treatment of typhus fever in certain countries, especially in Europe. In my opinion the routine employment of alcohol is not to be recommended. The vogue which this has had at certain periods, based upon the undoubted good results obtained, was due to the circumstances under which the disease occurred, that is to say, during or immediately after a great war and in people worn out by hunger, fatigue, or privations. It may easily be understood that under such circumstances the treatment of all patients indiscriminately by alcohol, which stimulated the nervous system and increased the strength, would be found to be an efficacious measure and productive of the best results. Under ordinary circumstances, however, the employment of alcohol should not be regarded

as a method of treatment of the disease, but rather as applicable in individual cases only and to meet certain indications furnished by the patient. The latter, when in poor condition in consequence of previous disease, of overwork, or of extreme age, requires alcohol, and in these conditions Mexican physicians have prescribed it with benefit.

From the formulating of this general rule we may pass to its application in special cases. Alcohol is to be given early and throughout the entire course of the disease in the case of individuals who have used it freely in health, and the quantity employed is to be regulated according to the patient's previous habits in this regard. In the aged alcohol must be prescribed as soon as adynamia appears, and its use is then to be continued throughout the disease. If the pulse becomes small, weak, intermittent, compressible, or irregular, alcohol is indicated; but if the character of the pulse does not improve after a reasonable trial the remedy is to be discontinued (Murchison). A pulse of abnormal slowness also calls for the same remedy. It is necessary, however, not to trust exclusively to alcohol to restore the rhythm of the heart's contractions, but we must have recourse also to those agents which act directly upon the circulatory system and to which we referred above when speaking of the measures suitable for stimulating the functional activity of the kidneys.

Fever.—This is an essential element of the disease. Its function is to destroy the infectious materies morbi, and we must not ordinarily attempt to overcome it by therapeutic measures; the office of the physician is only to moderate it on occasion, in order that in itself it may not become a cause of the death of the patient. This will suffice to explain why we do not recommend the antipyretics as remedies to be employed against the disease, but simply as regulators of the fever. When the latter remains for several days above 40° C. (104° F.), and especially if it mounts to 41° C. (105.8° F.), steps must be taken to reduce it. Antipyrin, antifebrin, kairin, etc., reduce the temperature, but in large dose or when the remedy is continued for a length of time it disturbs the rhythm of the heart and reduces functional activity, thus constituting a danger, since, as we have said, these changes in the circulatory apparatus are signs of bad omen. There are more innocuous measures for reducing the temperature, namely, those which increase the urinary excretion, and the physical remedies, such as sponging of the skin, cool or cold baths, and enemata of water at a temperature below that of the body; these abstract heat from the body without producing disturbances in the functions of the vital organs. While we recommend sudation by means of the remedies mentioned above, we are not advocates of the

use of pilocarpine except in cases of very extreme elevation of temperature when it is desirable to obtain a rapid, even though not permanent, reduction of the pyrexia. Enemata of boiled water containing borax in solution in the proportion of four per cent., or permanganate of potassium (1:10,000), and at a temperature of 15° to 20° C. (59° to 68° F.), serve not only to reduce the temperature but also to empty and disinfect the intestine. Enemata of oxygenated water (ten per cent.) at a temperature of 12° to 15° C. (53.6° to 59° F.) fulfil the first of these indications excellently, for they lower the temperature directly and also promote greatly the process of oxygenation. In support of this assertion I will quote briefly what Bouchard has to say on this point: "Better than precipitating the toxic substances is to stimulate the organism to burn them in the blood and the tissues, by supplying it abundantly with oxygen. I have shown that this is possible, for in proportion as oxygenation is increased the toxicity of the urine is diminished, and it is in this fluid that the toxins, which are the normal products of the vital activity of the cells of the body and of the intestinal microbes, are excreted."

Another means of reducing the temperature is bathing. We may use baths, as I have before said, to promote the functional activity of the skin and to abstract heat, restoring in this way to the liver the power of destroying poisons and reëstablishing the formation of glycogen, which had been arrested by the fever, of that glycogen which is used by the hepatic cell in its action of destroying toxic substances, as Roger has demonstrated in a notable thesis. The mode of employment of baths has varied greatly at different times, and a description of all the different methods does not come within the scope of an article of this nature.

The baths differ among themselves greatly according to the temperature of the water and the manner in which this is applied. They may be cold or tepid or begun at a moderately high temperature and gradually refrigerated; the water may be applied in the form of sponging, affusions, the wet pack, or the tub bath. I shall say a few words only as to certain special modes of administering baths for the reduction of high temperature.

Tepid baths are employed, either continuously, the patient being kept in the water at a temperature of 31° C. (87.8° F.) for a period of twenty-four hours, as recommended by Riess; or the temperature of the water is reduced from 5° to 20° C. (9° to 36° F.) below that of the patient, and the latter is placed in the bath whenever his temperature reaches 40° C. (104° F.) and removed again when he begins to be chilly—this is Ziemssen's method; or finally we may have recourse to Bouchard's method which is to give the bath in the beginning at a

temperature 2° C. (3.6° F.) below that of the patient, gradually reducing it to a temperature 30° C. (54° F.) below; the immersion is continued for an hour or more and the baths are repeated as often as necessary up to as many as eight in the course of the twenty-four hours. It will readily be understood that these different methods of bathing find their application in the different conditions which we have described above, but they are not to be regarded as special methods of treatment in all cases. Furthermore, bathing is not a remedy of easy application in daily practice, for it requires the presence of intelligent nurses, and is out of the reach of the very poor.

The cold bath has acquired such a vogue and enjoys such a reputation, administered after Brand's method, that I am under the necessity of adding a few words concerning it. I shall follow chiefly Bouchard's description." The method consists in bathing the patient every three hours, day and night, in water at a temperature of 18° C. (64.4° F.), each bath being of from eight to ten minutes' duration. The patient is very gently placed in the tub in such a manner that the water covers him completely as far as the shoulders. At the moment of entrance into the bath the patient experiences a severe chill, but this lasts only a moment; at this time an acidulated drink containing wine or cognac is to be administered. During the continuance of the bath a fine jet of water at a temperature of 18° or even 10° C. (64.4° or 50° F.) is directed against the nucha; at the same time friction or massage is made of the entire body. At the end of ten minutes, more or less, the chill returns and this is an indication that the bath should be terminated. Another potion of wine or brandy and water is given to the patient, who is carefully removed from the bath, covered up, and left to repose until the chill has disappeared; when this happens he usually falls asleep. In the intervals between the baths the body is covered with cold compresses, while warm compresses or even hot bottles are applied to the lower extremities. The temperature of the patient is taken every fifteen minutes and whenever the thermometer indicates 39° C. (102.2° F.) a new bath is given. In mild cases fifteen or twenty baths are given in a period of five or six days. In cases of moderate severity the number of baths is increased from forty to sixty, half of them during the first week.

In very severe cases the "intensive" method is employed. This consists in placing the patient in a bath at 26° C. (78.8° F.), the next one at 24° C. (75.2° F.), another at 22° C. (71.6° F.), and so on, until we reach 18° C. (64.4° F.) or even 15° C. (59° F.). Affusion is made with colder water, at 10° C. or even 8° C. (50° or 46.4° F.), until a severe chill comes on. During the continuance of the bath,

massage or frictions of the body must be performed without intermission. The second chill comes more quickly, within eight minutes or less. The patient is then removed from the bath under the same precautions, but instead of cold compresses an ice bag is used. If the heart is weak another ice bag is placed over the precordial region. If the symptoms increase the bath is repeated every two hours; if they become less pronounced the method of bathing indicated for mild cases is resorted to.

As may be seen from what has preceded, this method of treatment has for its object to lower the temperature of the patient while stimulating powerfully the functions of the skin and of the internal organs and provoking diuresis by means of the bath itself, of abundant drinks, and of internal stimulants, such as wine or other forms of alcohol; in this way we stimulate the renal functions, a measure upon the necessity of which we have already so strongly insisted.

I do not possess any statistics in regard to the value of cold bathing in the treatment of typhus fever. In typhoid fever, however, the mortality under this method has varied between four and nineteen per cent. in the hands of different practitioners, but taking an average of all the cases reported by the partisans of this method, we find that the mortality ranges from eight to eleven per cent. This would be a very good result could we accept the figures unreservedly and were it possible to do away with all the objections which have been advanced by those who oppose the method.

In conclusion we may sum up in the words of Brouardel concerning the action of the baths which are to be employed in grave cases: "The cold bath lessens cellular disintegration, favors antisepsis and nutrition of the skin, and promotes diuresis and elimination; it has a tonic and calmative effect upon the heart, prevents the terrible results of hyperpyrexia, and, finally, seems to increase the phagocytic action." It may at first sight appear strange to reduce to this one method the treatment of grave infectious diseases, but we see that it is in reality a good physiological and antiseptic method of treatment.

The *severe form* of typhus fever is one of the most terrible diseases that the physician ever encounters in his practice; its treatment does not differ in nature from that which we have just been discussing, but it demands on the part of the physician very careful observation in order to determine the circumstances that increase the gravity of the disease so that he may be able to prevent them if possible, to detect the first signs of any complications, and to recognize any disturbance of function on the part of the vital organs and remedy it as soon as possible. While in the benign form the skill of

the physician is not severely taxed, in the grave form he is obliged to exercise all his sagacity, his vigilance, and his energy to combat any untoward accidents, and must be endowed with a tireless perseverance to contend up to the very last; typhus is, as we have seen, a cyclic disease, and if the physician succeeds in maintaining the strength of his patient up to the period at which the disease naturally subsides, the life of his patient will be saved.

As we have so many times insisted, it is very necessary to be on our guard against the *complications* which may occur on the part of the digestive, respiratory, circulatory, and nervous systems; to watch for the changes in nutrition as manifested by bedsores; to detect the first appearance of parotiditis and otitis, which come on at the beginning of convalescence; and, above all, to detect and treat phlebitis and arteritis, which may lead to gangrene of the extremities. We cannot enter into more details regarding the symptoms which correspond to each one of these complications, nor in regard to the various measures which their treatment demands, for such a study would carry us beyond the limits assigned to this article.

Convalescence.

The management of the patient during convalescence from typhus fever calls for special care on the part of the physician. The rapid return to health and the necessity which the organism feels of restoring the lost strength arouse the appetite which sometimes becomes voracious. The diet must, however, be increased very gradually, the food must be given at proper intervals, and the physician must himself select the most easily digested articles.

We should not permit the patient to sit up too early for fear of syncope, nor should he leave the bed until he has recovered in a measure his strength. He should take a bath for cleansing purposes as soon as the condition of his strength will allow.

The physician, finally, should never lose sight of his patient until it is certain that none of the complications above mentioned can occur and until the organism has recovered its normal functions.

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PLAGUE.

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PLAGUE.

Synonyms.—Pestis, Pestis bubonica, Bubonic plague, Black death.

Definition and History.

Plague is an acute infectious disease, characterized etiologically by the presence of a specific microbe, and anatomically by certain pathological changes in the lymphatic nodes. This disease was described by Rufus of Ephesus as having existed in Lybia, Egypt, and Syria as early as the third century before Christ. Earlier accounts are quite untrustworthy, inasmuch as the word λοιμός was used by ancient authors to denote any pestilence attended with a high rate of mortality. For instance, Thucydides gives a history of the Athenian pestilence, but as no mention is made of any enlargement of the lymphatic glands, the nature of the disease has been called in question.

The first epidemic of historical importance is the one which broke out in the reign of Justinian, known as the "Justinian plague." The epidemic originated in Egypt about the year 542, and passed through Constantinople to reach Liguria, Gaul, and Spain, from whence the disease was imported into Marseilles in 588, and ultimately spread over all Europe. The mortality must have been enormous in this pandemic, which lasted through half a century. In Constantinople alone over ten thousand people are said to have perished in one day (?). The pandemic of the fourteenth century was also one of the most extensive pestilences that the world has ever witnessed. It was then that the malady was generally known as "black death." Another designation, "pestis inguinalis," also appears in some of the contemporary writings. The pandemic is supposed to have originated in China about the year 1334, and, spreading through India and Persia, reached Europe in 1347. It prevailed in Russia, Germany, Italy, and France, reaching England in 1349 and Norway in 1351. The mortality figures in all these countries are far from being reliable, but we can form some idea of the magnitude of the epidemics when we read that in many cities more than half of the population was

swept away. The entire number of deaths in Europe during this visitation is estimated to have been over twenty-five millions, and perhaps as many more perished in Asiatic countries.

It is said that as many as thirty minor epidemics appeared in different parts of Europe between the eleventh and fifteenth centuries (Proust), but the next epidemic of any importance was that of Marseilles in 1720. The disease was brought over from Syria in an infected vessel, and 86,000 persons fell victims to the scourge. During the years 1770 and 1771, 80,000 persons died of the plague in Moscow. This epidemic is believed to have started in the neighborhood of Jassy, and to have come through Kieff in order to reach Moscow.

Coming down to the beginning of this century, we find that Constantinople was the seat of two severe epidemics—one in 1803, with 150,000 deaths, and another in 1813, with 110,000 deaths (Proust). Subsequently there were several outbreaks in the Balkan peninsula between the years 1814 and 1841. The plague in Greece in 1828 may be said to have been one of the most conspicuous among them. An isolated outbreak in the southern part of Italy (Noja), in 1815, perhaps deserves mention in this connection.

The last of the European epidemics was that of Vetlianka in the Astrakhan government in Russia in the winter of 1878–79. It is supposed by some that the disease was imported from the provinces about Recht, on the southern shore of the Caspian Sea, not directly to Vetlianka, but first to the city of Astrakhan some time in the year 1877. There it manifested itself in a most benign type (*peste fruste*). From one hundred to one hundred and fifty persons are said to have been attacked, without there having been a single death (?). It is further assumed that the malady developed a malignant aspect after reaching Vetlianka.

Contrary to the above theory, Hirsch and Sommerbrodt are inclined to assume that the malady was imported in the articles (presumably booty of war) sent back from Armenia by the Vetlianka Cossacks. The writers were driven to this conclusion from the fact that the outbreak antedated the return of the troops themselves by a few days, and also that there was no case of plague in the Russian army during the campaign. The above-mentioned authors dwell on the relatively good hygienic condition of the town, to dispel any supposition as to the possibility of the autochthonous development of the malady. This epidemic did not assume any great dimensions; there were three hundred and seventy-three deaths in Vetlianka, and twenty-four in the neighboring towns.

Thus Europe has been free, for the most part, from large epidemics for a long time, but the ravages of the disease have not abated

in Africa and especially in Asia. For instance, in Egypt there were as many as twenty-one epidemics between 1783 and 1844. In 1858 there was an outbreak in Tripoli and another in 1874. In Arabia there is one mentioned as occurring in the same year. In the valleys of the Tigris and Euphrates a great outbreak took place in 1773, and several minor ones are subsequently recorded down to the Bagdad plague in 1876. After that there is an almost unbroken plague record up to 1895. The plague in Persia has also a long history; that of Recht (1876–77) has been already referred to, in connection with the Astrakhan epidemic.

In India, the plague seems to have long existed endemically, especially in the district near the Himalaya mountains. Reliable accounts thereof date only as far back as the year 1815, when there was an outbreak in Guzrate. Subsequently there was a severe epidemic in Pali in 1846. Minor epidemics are said to have been almost continuous in the hill districts, but they never attained any magnitude so that the attention of the English physicians was not particularly directed to them. Pearson and Francis laid great stress on the prevalence of a pleuropneumonic process in the Indian plague, and it seems that the glandular enlargement did not form a conspicuous part of the clinical picture. It is for this reason mainly that Hirsch was led to doubt the identity of the Indian plague with that of the Levant. In this connection it is interesting to observe that it was in Bombay that the existence of the pneumonic plague was established by Professor Childe. The nature of the earlier pestilences of India may perhaps be cleared up, in some measure, by the investigation of the present form of disease in the districts near the Himalayas, where it exists endemically.

Some have been inclined to trace the origin of the present epidemic in Bombay (1896–97) to a recrudescence of these endemics, but importation of the disease from China seems more probable.

Our knowledge of diseases in the Chinese empire is very incomplete. We can only surmise that the plague existed there endemically from time immemorial. Nevertheless we have some scattered records of the great outbreaks in 1850, 1866, 1871, and 1872. At present the regions of Yunnan, Pakhoi, and Lienchu may be regarded as the plague districts. In 1894 the disease made an advance into Canton and Amoy, and from thence into Hong-Kong. The Hong-Kong epidemic (1894) is memorable especially as being the one in which the discovery of the pathogenic bacillus was made. There were forty-four cases of plague in Hong-Kong during the ensuing year. These cases may have been due to the recrudescence of the epidemic of 1894, or they may have been due to reimportation. Atkinson is inclined to

the latter view, and states that the first of these cases occurred six months after the cessation of the last epidemic. The epidemic of 1896 was the continuation of that of the previous year, and in fact the plague maintains its hold there even now.

Since the concession of Formosa to Japan, cases of plague have been almost uninterruptedly reported, and it is very probable that the disease has existed there a long time.

Etiology.

In old times the displeasure of supernatural beings was assumed to be the causative factor of various pestilences. In the middle ages the Israelites suffered frequently from the charge of having poisoned the drinking-waters, in order to produce an outbreak of plague. Coming down to more rational times, climatological, meteorological, and telluric influences have been looked upon as the causes of the disease. Further, the appearance of the plague has been ascribed to war, famine, overcrowding, earthquakes, inundations, or a diseased condition of the grain and other food supplies.

It has been established beyond all doubt that the concurrence of any or all the above-mentioned factors can never produce a case of plague. They can therefore be regarded as being merely predisposing factors, but possessing in themselves no primary influence in the production of this malady. The devastation produced by plague, and in fact by all the infectious diseases, is usually severest in unsanitary districts, and among the poverty-stricken and ignorant.

Race, age, and sex seem to make no difference in the liability to the attack. Certain occupations were formerly believed to confer immunity against plague, but in the light of modern knowledge such supposition can no longer be maintained. On the other hand, certain occupations, such as that of a rag-dealer, may increase the risk of infection.

One attack of the disease seems to confer immunity against a subsequent attack.

Individual predispositions would be increased by all those influences which tend to diminish the vitality of the system, but in a given case of infection more importance is to be attached to the risks of infection to which the individual is exposed; and also it is to be borne in mind that this risk of infection may be greatly increased by a number of accidental circumstances which cannot always be foreseen and guarded against.

BACTERIOLOGY

The plague never occurs spontaneously in a locality in which the malady has not previously existed, but each case is always derived from a previous one. Reasoning from analogy, Virchow predicted the discovery of the microbic origin of this disease, which prediction, as we shall see, was realized in the year 1894. As early as the year 1879 Hirsch and Sommerbrodt made mention of innumerable refractile granules in the blood of the patient, which granules often arranged themselves in pairs and occasionally appeared elongated. But they did not seem to attach any great etiological importance to these bodies.

In 1894 a scientific commission for the investigation of plague, directed by Aoyama and Kitasato, was sent from Japan to Hong-Kong, where the writer (Kitasato) was able to isolate the bacillus which is the specific cause of the malady. The bacilli were found constantly and almost in pure culture in the blood, in the tissue fluids, and in the enlarged glands of those who had died of the plague, and also in the blood obtained from the finger tip of the living. The same microbes were also demonstrated in the intestinal contents after death from the plague. We might add further that the same organisms were met with in the bodies of rats and mice found dead during the period of the epidemic.

The constant presence of a characteristic microbe in plague justifies the conclusion that it is the causative agent of the disease, and this position is further confirmed by animal experiments, in which it has been shown that inoculations of pure cultures of the bacillus and of the plague material, *e.g.*, the pulp of the enlarged glands, produced identical results. This microorganism should therefore be designated "bacillus pestis."

The microbe is rod-like in shape and rounded at both extremities. In the preparations made from the blood or the fluids of internal organs, the poles of the bacilli are stained more deeply than the central portion, giving an appearance similar to that of the bacillus choleræ gallinarum. In the glands, although many of them appear like diplococci, there is a considerable number of the same microbes, which, staining easily in the middle portion, present distinctly bacillary forms. In the lungs, heart, brain, and spinal cord it is not rare to find them presenting an appearance like that of streptococci. Again, in artificial cultures the streptococcus-like appearance is the rule. On attentive observation, however, these cultures will be found to consist of bacillary chains and not cocci groups. On the other hand, cultivations on solidified serum present the real rod-like shape.

The plague bacilli take all the aniline stains, and they are not decolorized by the application of Gram's method. They are endowed with motility which is not very active, but which should not be mistaken for molecular movement. In order to observe their motility it is best to study them in a medium at the temperature of 37° C. In the specimens prepared from blood or tissue fluid of various organs, and also in cultivations on solidified serum, the bacilli are seen to possess distinct capsules. In other artificial cultivations the capsules are not developed.

While on the one hand the unstained middle portion gives the bacilli a close resemblance to diplococci, it produces the impression, on the other hand, as if there were a spore formation in these microorganisms. Simple examinations will, however, make it evident that the plague bacilli do not possess any of the attributes of the spore-forming bacteria.

The plague bacilli seem to be particularly prone to undergo degeneration of form in artificial cultivations, specially in the fluid media. Spheroid, ovoid, dumb-bell, and huge rod-like forms are the more frequent of these involution forms.

When cultivated on solidified serum, the growth of the microbes is visible after an incubation of fifteen to twenty-four hours. On surface view the colonies are rather moist and of a gray (slightly yellowish) hue, but by transmitted light they are seen to possess a bluish tint and are quite transparent. The individual colonies never attain a large size, and when kept in the incubator for more than four days they disappear, perhaps leaving a faint trace behind. Observed under the microscope the individual colonies are circular in shape with irregular margins. They appear granular at first, but afterwards they become relatively denser in the centre, where the color is quite brown (seen under the microscope). The culture medium is not liquefied by the growth of the microbe. On agar the mode of development is entirely similar to that on serum.

The multiplication of the microbes in gelatin is extremely protracted, taking four or five days at the temperature of 20° to 25° C. In order to observe the isolated growth, it is advisable to make isolation cultures in the upper portion of gelatin media (containing fifteen per cent. gelatin and two per cent. glucose). The colonies are then seen to be spheroidal in shape, with slightly irregular superficies, and grayish in color. The growth in the stab culture presents an appearance very much like that of streptococci, and, as in the case of the latter, there is no formation of the film layer over the free surface of the culture medium.

Bouillon is made uniformly turbid at first by the growth of the

microbe, but subsequently fine flocculi are formed and there is sedimentation at the bottom of the test tube. In sterilized milk the growth of the plague bacilli is attended with the coagulation of the medium at the end of the second day. On potatoes a thin film-like growth of somewhat desiccated appearance is observed at 37° C.

The plague bacillus is a facultative anaërobe. In fact its growth is more vigorous in anaërobic cultures, and in such its virulence is preserved for an almost indefinite length of time. Cultures as old as eight to ten months have been found to possess their original virulence. The optimum temperature is between 36° and 39° C. The bacilli do not produce pigment or gases.

Laboratory animals, such as mice, rats, guinea-pigs, and rabbits, are all susceptible to infection. They sicken in the course of from twenty-four to forty-eight hours after inoculation, the temperature rising as high as 41.5° C., and they die within from two to five days, according to their size and the quantity of the virus inoculated. Examined after death, the parts around the site of inoculation are seen to be infiltrated with hemorrhagico-gelatinous exudations, the spleen is enlarged, and often there is a tumefaction of the lymphatic glands. The bacilli are found in the blood and consequently in all the organs. Experimental infection by way of the digestive canal can easily be produced, and the animals fed with the virus succumb under exactly the same conditions as do those inoculated. Inhalation experiments have thus far been attended with negative results. Pigeons are not susceptible to plague infection.

The preservation of the virulence of the microbes in anaërobic cultures has been adverted to above. In aërobic cultures the virulence is lost rapidly, so that when left in the incubator for from three to four days the bacilli are found to be deprived altogether of their pathogenic action, and perhaps of their vitality as well. If the cultivation is allowed to remain in the incubator for a day, and is then removed therefrom and kept in a cool place, the virulence may be preserved for a week or two, but seldom longer. The bacilli undergo attenuation if they are cultivated through several generations in artificial media. The cultures ought therefore to be kept reïnvigorated by constant passages through the animal organism.

That the bacilli produce toxin in artificial culture is evident from the fact that sterilized (at 60° C. for twenty minutes) bouillon culture is found to possess toxic properties. But the quantity required to produce fatal intoxication with sterilized cultures is ten times that which is necessary to produce fatal infection with the unsterilized.

In order to form a correct notion of the vitality of the plague microbe and the consequent extent to which disinfection should be

carried, it is necessary to study the resistance of the microbe to the action of physical and chemical agencies. It was found that, when the contents of a bubo were spread out in thin layers on cover-glasses, and left to dry, all the bacilli had died by the end of the fourth day. A temperature of 80° C. was sufficient to destroy their vitality in thirty minutes, and in the steam sterilizer they were found dead after a few minutes. If to the bouillon culture of plague bacilli carbolic acid be added to make the solution of one-per-cent. concentration, the bacilli will be found dead at the end of an hour. With one-per-cent. concentration of lime the result is identical, but a one-half-per-cent. concentration of the latter is not efficacious till after a little more than three hours.

It is an important point to determine whether the diagnosis of plague can be made by the bacteriological examination of the blood taken from the finger tip. We have been able to demonstrate the presence of the microbes in blood twenty-five times out of twenty-eight cases examined, and we therefore are of the opinion that the finger-blood examination would be decisive in the majority of cases. A fair degree of bacteriological expertness, however, will be necessary to make the results reliable; for in some cases, the number of bacilli is extremely small, so that several slides have to be examined before one can arrive at a positive result. Examination of the fluid aspirated from the glandular swelling may perhaps afford an easier method.

We come now to consider the mode of infection. We have observed many cases in which infection through the respiratory organs could be fairly presumed. Still the most common way must be that of inoculation through external wounds. The fact that the microbes were found in the intestinal contents, and the positive results of the artificial infection by feeding, would lead us to admit the possibility of infection through the ingesta.

Experimental researches show that animals can be made immune against the bacilli of this disease by preliminary injections of the attenuated virus. The same result is obtained by the injection of sterilized (at 60° C.) virulent cultures. In order, however, to produce a great quantity of antitoxin in the blood of animals, they have to be "hypervaccinated" by repeated injections of large doses of fresh virulent cultures. The serum of these hypervaccinated animals is demonstrated to possess antitoxic properties. For instance, 1 c.c. of the serum injected into the subcutaneous tissues of a guinea-pig will be found sufficient to neutralize three to four times the fatal dose of the fresh culture injected simultaneously. Furthermore, the serum is endowed with curative efficacy. Experiments have shown that the serum injected twelve hours after the inoculation can save guinea-

pigs which would otherwise be certain to succumb to the infection within forty-eight hours.

Yersin's Bacillus Pestis.—It has been quite generally assumed that the bacillus above described is identical with that of Yersin, but this assumption is incorrect. The two are quite distinct, as may be seen from the following summary of their differences: To avoid tiresome repetition we shall designate Yersin's bacillus as YB, and Kitasato's as KB.

YB is much larger than KB, and does not possess the distinctly diplococcus-like appearance of the latter. Owing to its polymorphism exact measurements are difficult to give. It does not possess a capsule. (We might mention in this connection that the photogram of Zettnow must not be considered as representing a capsule, in the general acceptation of the term.) YB is not motile and is decolorized by Gram's method. Cultural differences are equally conspicuous. On agar the growth of YB is extremely luxuriant, and though the growth is rather slow at first it continues for a week, forming creamy white, opaque colonies projecting a good deal above the level of the surface of the media. Very young colonies are small and quite transparent. On the other hand the colonies formed by KB are extremely delicate, transparent, small discs which attain the size of a pinhead, and cease growing and then disappear on the fourth day of incubation, presenting in all these respects a close resemblance to the growth of diplococcus pneumoniæ. Bouillon is not made uniformly turbid by the development of YB; further, milk is not coagulated by the growth of YB. The above-mentioned differential points ought to be enough to distinguish the one from the other. It is curious to observe that Yersin states that his plague bacilli (YB) are found in the blood only in foudroyant cases, while Kitasato maintains that the bacilli (KB) can be found constantly present in the blood, and further that they may be found in the blood of convalescents for from three to four weeks after the symptoms have subsided.

Further bacteriological investigations of the plague are desirable, since it is necessary that the scientific world should come to some definite conclusion as to the etiological bacilli, before orrhotherapy and preventive inoculation can be instituted on a truly rational basis.

Pathological Anatomy.

Rigor mortis is very pronounced and sets in early. Often there is a marked post-mortem rise of temperature. In a case reported by Aoyama, the rectal temperature was taken four hours after death, and the thermometer indicated 43° C. (109.4° F.), which was as high as

the instrument would register. Petechiæ and subcutaneous extravasations are not frequent in modern epidemics, although they must have been very conspicuous in the earlier ones. The presence of furuncles, carbuncles, etc., has already been adverted to. Emaciation is not marked in rapidly fatal cases.

We have already described the localizations of the external *buboes*. The swelling of the internal lymph nodes is, as a rule, consecutive to that of the external ones. For instance, the enlargement of the cruro-inguinal glands is often followed by the same process in the iliac, lumbar, or hypogastric glands. These latter may, however, be the seat of a primary localization, but such cases must be extremely rare. Other nodes in the peritoneal as well as in the pleural cavities may be secondarily affected. That the mesenteric glands may be the seat of primary localization is questioned by most authors, although some are inclined not only to admit the possibility of this, but even claim that such primary localization proves the intestinal origin of those cases.

The formation of primary buboes is due to the following factors (Aoyama): Hyperæmia and dilatation of the blood-vessels, and in some cases hemorrhage, exudations of an inflammatory nature, hyperplasia of the cellular elements, and lastly the enormous increase of the specific microbes in the substance of the glands. On section, therefore, they are found congested and succulent, presenting at times hemorrhagic extravasations in their substance. Their consistence is diminished, especially towards the period of suppuration. Plague bacilli are found therein, sometimes in pure culture, or they may be associated with other bacteria. According to Aoyama these associating microbes, micrococci and streptococci, are to be regarded as the causative agents of the suppurative process. The periglandular tissues are found infiltrated with gelatinous and hemorrhagic exudations, and there is an abundant growth of the plague bacilli. Inflammatory changes in the periglandular tissue make the buboes immovable under the skin, and the consecutive suppuration extends to these tissues.

Sometimes the buboes undergo resolution, especially in favorable cases. But usually suppuration is the natural outcome, and finally the suppurating glands rupture, leaving ulcers behind which take a long time to cicatrize. As has been mentioned above, a necrotic process may be superadded.

Inflammatory processes of a similar nature are observed in all the lymphatic structures, for instance of the mouth and pharynx, and especially in the lymph follicles of the intestines and stomach.

Nervous System.—The dura mater is congested and the pia mater

may be the seat of extensive and pronounced œdema; there may also be some extravasation of blood into the arachnoidea. The brain and spinal cord are hyperæmic and somewhat œdematous; but hemorrhages are rare. A case of hemorrhage into the medulla, causing extreme dyspnœa, and another case of hemorrhage in the pons, have been reported by Aoyama. The ventricular as well as the cerebrospinal fluid may be increased in quantity.

In the *blood* there is great increase in the number of the leucocytes, a fact to which attention has been directed by Hirsch and Sommerbrodt. The increase may reach twenty times the normal number (Aoyama), while, on the other hand, the erythrocytes are not diminished. There is, however, a diminution in the quantity of hæmoglobin. The occurrence of extravasations under the skin and in and around the glands has already been noted. They may also be observed in the mucous membranes, in the muscles, in the sheaths of the nerves, in the adventitia of blood-vessels, under serous membranes ("subcapsular"), into the serous cavities, and in the substance of some of the viscera. The erosion of large vessels has been adverted to above.

The *heart* is usually dilated, especially the right ventricle.

The *muscles* are anæmic and flabby, and the seat of parenchymatous degeneration, which in some cases is associated with fatty infiltration.

Respiratory Organs.—There are catarrhal changes in the larynx which may be found œdematous, especially if the cervical buboes are developed. Catarrh of the bronchi is very often noticed, but it is not severe in character. The lungs are œdematous and hyperæmic, and hypostatic congestion is marked. In pneumonic plague, we meet with foci of broncho-pneumonia, surrounded by a zone of congested pulmonary tissue. In some cases the alveoli are found filled with sanguinolent fluid swarming with plague bacilli, but without noticeable pathological changes in the pulmonary parenchyma. Multiple abscesses and pulmonary infarcts have been occasionally noted. Pleuritic changes are observed in the pneumonic cases, and also in patients having primary buboes in the axilla.

Catarrhal changes in the *stomach* are almost constant and well marked. Ecchymoses are frequent, but larger hemorrhages are rare. Croupous inflammation is exceptional (Aoyama), but ulcers are sometimes found.

Hyperæmia, ecchymoses, and catarrhal changes are present in the *intestines*, and the swelling of the lymphatic structures here is well marked. The mesenteric glands are swollen and congested, and there may be hemorrhage into the folds of the mesentery.

The enlargement of the *spleen*, which is almost constantly present and pronounced, may become quite considerable; the organ may attain from two to four times its normal dimensions. On section the pulp is found congested and soft, and even diffluent in many cases.

The *kidneys* are congested and enlarged at times, and the convoluted tubules are particularly the seat of parenchymatous degeneration. Here again fatty changes may be superinduced. The mucous membrane of the pelvis is very often the seat of numerous ecchymoses, perhaps at times of more serious bleeding. Punctiform hemorrhages may be found on the mucous membrane of the bladder, and this viscus may be either contracted or distended with urine.

The *liver* is enlarged and hyperæmic, the hepatic cells have undergone cloudy swelling, and the blood-vessels are dilated. Abscess is rarely observed, and still more rarely do we meet with multiple necrotic points in this organ (Aoyama, German commission).

The pancreas, thyroid glands, and salivary glands are always found normal.

The specific bacilli are found in the organs above mentioned, and particularly in the necrotic foci.

Aoyama lays great stress on the presence of streptococci in the blood, and consequently in the sections prepared from the different viscera. These streptococci may be regarded as the cause of the septicopyæmic condition that is sometimes added to the clinical picture of this malady.

Symptomatology.

The various clinical forms of this malady may be grouped under three types, viz.: (1) Glandular or bubonic plague; (2) pestis siderans, otherwise called plague septicæmia; and (3) plague pneumonia. The dividing lines between these forms are not to be considered as absolute and definite, neither is it to be understood that all these three enumerated types are brought out into prominence in all the epidemics. For instance, the pneumonic plague was not observed in the Hong-Kong epidemic of 1894. We shall begin by describing the more usual form of plague, to wit, the glandular type, the symptomatology of which may be studied according to the following sequence: (*a*) the period of incubation; (*b*) the prodromal period; (*c*) the invasion; (*d*) period of fastigium; and lastly (*e*) the period of convalescence.

Period of Incubation.

Aoyama fixes the duration of the incubation period as being between two and seven days. According to Hirsch and Sommerbrodt

it is from two and a half to eight days, the average duration being five and a half days. Lowson mentions a case in which the incubation could not have been less than nine days.

Prodromal Stage.

In some cases prodromes may be entirely absent, or they may be so slight as not to have been noticed by the patient himself. When present, they may last for a few hours only, or the period may extend over two or three days, during which time the patient feels dull and unwell, and has headache and vertigo. He usually loses his appetite, and may suffer from nausea, but vomiting is rare. Exceptionally there is diarrhœa during this stage. Pain and stiffness in the joints have been noted, and the patient may also complain of chilly sensations and sometimes of palpitation. But of all the prodromes, the one having the greatest significance is the tenderness and pain in the inguinal or axillary region, predicting, so to speak, the subsequent affection of the lymphatic nodes in these parts.

Invasion.

The invasion is characterized in many cases by pronounced chills, sometimes by rigors or by a subjective sensation of heat. In some epidemics the initial chill is absent or occurs very infrequently. Mental and physical prostration is extremely severe from the outset. Headache is usually quite severe; nausea and vomiting or diarrhœa may be present. These symptoms may last for few hours or for several days, before the fastigium is reached.

Fastigium.

When the disease is fairly established, generally on the second day, we may note the following symptoms:

Temperature.—The rise of temperature is rapid, the thermometer registering from 39° to 40° C. (102.2° to 104° F.) on the day of invasion or within thirty-eight hours thereafter. Hyperpyrexia (41.5° C.= 106.7° F., and above) is not infrequent and constitutes an unfavorable element in prognosis. There are also cases of an extremely gradual rise of temperature which may not reach its maximum until as late as towards the end of the fourth day of the disease.

In very light cases the fever continues for three or four days, and the recovery may be marked by critical defervescence with profuse perspiration. In cases of moderate severity the febrile movement may continue for a week or more, and in many cases it may extend

over three weeks. The course of the fever is continuous in type at the beginning, but later it may assume a remitting or irregular course. The temperature curve of the latter description, when pronounced, is due in many cases to the pyæmic condition or to other complications. Rarely we have irregular fever from the outset.

Lymphatic Nodes.—Tenderness, pain, and possibly swelling of these lymphatic ganglions may be noticeable even during the *stadium invasionis*. Usually, however, they become conspicuous on the day following that of invasion. But sometimes it happens that the tumefaction is delayed till the third, fourth, or even sixth day of the disease. As to the localization, it may be stated that the crural and inguinal groups are most frequently attacked (seventy-five per cent.), the swelling being situated 4 to 5 cm. (1½ to 2 in.) below Poupart's ligament. Next in frequency is the localization in the axillary region (ten per cent.), with the consecutive enlargement of the supraclavicular chain. Rarely the cervical, jugular, submaxillary and suprahyoid, occipital, or some other groups, may be primarily affected. Griesinger states that in children the submaxillary glands are very often affected. Usually it is a single group of glands that are inflamed, but bilateral or multiple involvement has been observed. It may happen, though rarely, that the minor chains are the seat of the primary localization, while the more important glands remain comparatively unaffected. A diffuse swelling in the hypogastrium points to the involvement of the iliac ganglia. We have to remember that in corpulent people a slight enlargement may be overlooked.

The enlargement advances rapidly so that in a day or two after its appearance the affected gland may attain the size of an egg or still greater dimensions. The swelling is not uniform among the individual nodes of the chain involved, one or two of them being usually especially prominent. Later in the course of the disease, after inflammation has been set up in the periglandular tissue, the contour of the individual glands can no longer be made out, and there results a diffuse swelling of large size.

Pain and tenderness are usually present and progressive, and may be so severe as to keep the patients awake at night.

In favorable cases resolution of the swollen glands occurs, but more frequently suppuration ensues. Unfortunately, however, many of the patients die before the glands are ripe for suppuration to take place. It is to be remembered that the pus formation does not take place till about the eighth or the tenth day of the disease, while the majority of the severer cases terminate fatally before the seventh day. Hirsch and Sommerbrodt state that in light cases sup-

puration may occur as early as the third day. Then again there are cases in which this process has been delayed for weeks.

In addition to the simple suppurative changes, a necrotic process may be established, producing sloughing of the glandular swelling. Such an event must be considered an extremely unpleasant complication. Other lymphatic structures, such as the tonsils or the follicles of the pharynx, may be involved in the inflammation.

Other external appearances have no pathognomonic importance. The *face* is flushed in the beginning, but soon becomes dull, assuming an anxious expression. Cyanosis is not infrequent, but jaundice is rare. The patients rapidly fall into the typhoid state and present the facies common to that condition. The eyes are bright at the beginning, with suffused conjunctivæ; the pupils are dilated or they may be unequal in some cases. In the latter case meningeal trouble may be inferred. The pharynx is congested, and the tonsils may present ulcerative changes.

The *skin* is usually hot and dry, but in mild cases there may be perspiration, particularly at the time of defervescence. Sudamina may be observed in the later days of the disease, but this is a rare phenomenon. Vesicles, pustules, abscesses, and carbuncles have been noted. The diagnostic and etiological importance of these lesions will be discussed later on. A very slight exanthem has been noticed in a few cases. Subcutaneous œdema is never observed, except in cases in which there is severe renal complication. If the patients live long the emaciation will become very marked.

Subcutaneous extravasations of great extent were often mentioned by the earlier writers, and on account of these, indeed, the name "black death" was applied to this malady. In modern epidemics the occurrence of petechiæ and extravasations is comparatively infrequent. Epistaxis, bleeding from the gums, hæmoptysis, hæmatemesis, hæmaturia, bleeding from the female genital organs, other mucous-membrane hemorrhages (*e.g.*, under the conjunctiva), and bloody stools are also rare phenomena observed mainly in very severe cases.

It is to be remembered that in some epidemics these symptoms are relatively infrequent, while in others they may come to the foreground of the clinical picture. Again, it is to be added that the symptoms may vary at different periods of the same epidemic. This is in fact the case in almost all the infectious diseases. Usually the cases are more grave at the beginning of an epidemic and also at its height, and become lighter towards its decline.

Nervous System.—Headache and vertigo are constant symptoms at the beginning, and the former may be very severe and persistent. On account of the extreme muscular weakness the gait of the plague

patient has been likened to that of a drunken man. This muscular weakness, together with the dazed condition of the patients, has occasionally been the cause of most serious accidents—for example, falling down a flight of stairs. In such cases they have even been taken to the surgical ward and treated there for fractures or wounds, until the appearance of the buboes revealed the true nature of the trouble.

Delirium is one of the most prominent symptoms and usually develops on the second day, and is usually much worse at nights. In light cases it is noticed only at night. The patient is troubled with hallucinations and may try to get out of bed, or may engage himself in a quarrel with the attendants. In most cases, however, the delirium is of low muttering type, but maniacal excitement is not infrequent. In other cases stupor and coma may prevail or may alternate with delirium. Again, there are some cases in which the mind remains quite clear throughout the course of the disease, and this may be the case even in severe attacks.

Pain in the loins, epigastrium, and elsewhere may be complained of. Hiccough may become very distressing and subsultus tendinum is observed in bad cases. Deafness may be due to the general obtunding of the sensorium, or may be the result of local disturbances. Strabismus may be noted. Stiffness of the neck and clonic convulsions are not common.

Digestive System.—Anorexia may be associated with nausea and vomiting, which latter, however, usually subsides in a short time, but in some cases it may become extremely troublesome through its persistence. The vomited matter may be watery, but is more often bilious in character; and though hæmatemesis is rare, there is frequently a slight admixture of blood. Intense thirst is complained of by some patients. Initial diarrhœa, when present, usually gives place to constipation, but there may be fetid and profuse diarrhœa throughout the course of the disease. Such diarrhœa is to be looked upon as an unfavorable element in the prognosis. The tongue is moist at first and coated with a white (sometimes chalky) layer in the middle, and with denuded edges, but it afterwards becomes dry, brown, and parched. According to Aoyama there is nothing which may be deemed characteristic in the appearance of the tongue in plague.

Circulatory System.—In the first day of the disease the pulse is frequent, large, but usually of good tension; it is often dicrotic. A feeble and irregular pulse is not infrequent, especially later in the course of the disease, and when this condition is pronounced it must be regarded with anxiety. The frequency ranges from 90 to 120; and in the worst cases it may run up to 130 or more.

Dilatation of the heart is frequent and can be easily demonstrated

by the increase of cardiac dulness. A systolic murmur may be heard at the apex and over the pulmonary orifice, but it is not due to the presence of any organic lesions.

Heart failure may come on at any time during the course of this malady and the possibility of it ought constantly to be kept in mind. Sometimes there is a warning of the impending danger, such as rapid and irregular pulse, cyanosis, and coldness of the extremities. But often it happens without the slightest premonitory symptoms.

Respiratory System.—The respiration is increased in frequency (40 to 50 in a minute). Slight bronchitis is not rare, but cough is not prominent. Dyspnœa may become distressing when there is enlargement of the cervical glands, and also if pulmonary œdema has become quite pronounced. Aoyama mentions a case in which extreme dyspnœa had no assignable cause until the autopsy showed a focus of hemorrhage in the medulla oblongata. Pneumonic symptoms are rare in some epidemics, while they are quite common in others. We shall discuss pneumonic plague in a separate section. Hæmoptysis is rare and observed only in the severest cases.

The *urine* is decreased in quantity, but suppression is rare. It may be clear or cloudy and brownish in color, and is usually albuminous. It contains indican and it does not present the diazo reaction. A slight admixture of blood in the urine is not infrequent, but copious hæmaturia is not a common occurrence. Microscopically hyaline and granular cylinders are to be observed.

Retention is very frequent and necessitates the use of the catheter, sometimes for a long time. Cystitis may develop consequent on the retention.

Liver and Spleen.—Sometimes the liver is found enlarged. Jaundice is rare, and when it is present it is catarrhal in nature, or it may be due to the pressure of the enlarged nodes on the excretory duct (Aoyama).

The spleen is found almost constantly enlarged as early as the second day, or perhaps the third. One must not forget, however, that in malarious districts the spleen might have been previously enlarged. Some complain of tenderness over the splenic region.

The above symptoms are due, no doubt, to the disturbance caused by the multiplication of the bacillus pestis in the organism, but at the same time some of them are due to the action of a toxic substance produced during the life process of the microbes. In one of the reports of the German commission to Bombay, we find an instance which seems to be quite conclusive on this point. It was a case of an aborted fœtus whose body was found free from the plague bacillus; but it had nevertheless absorbed from the diseased mother enough of

the toxic product to develop precisely the same pathological changes which form the basis of many of the symptoms described above. It should be added that a direct inference from the fœtal to the adult condition may be unwarranted.

Convalescence.

In very light cases the stage of convalescence is marked by crisis. As a rule, however, the defervescence in favorable cases takes place by lysis at the end of first or the beginning of the second week. Again, in severe cases, it is only after an anxious period of from three to five weeks that convalescence may be considered as fairly established. During convalescence there may still be a slight and irregular febrile movement. Emaciation and loss of strength are marked, and the cerebral functions are lowered for a long time. The period of convalescence may last from a week to a month or even more. Cicatrization of the glands may take weeks or even several months, and there may be fibroid induration after incomplete resolution. Convalescence may also be protracted by various complications or sequelæ.

Complications and Sequelæ.

Nephritic changes, when they become pronounced, are troublesome complications. It is, however, to be borne in mind that in some cases the so-called uræmic symptoms (coma, vomiting, convulsions, etc.) have been present, and yet at the autopsy very slight or almost no lesions of the kidneys were to be discovered (Aoyama). Retention of urine and the consecutive cystitis make the cases troublesome to treat. Pregnant women usually suffer from an abortion. Jaundice is rare; and when present it may be catarrhal, or may be due to compression of the excretory duct by the enlarged glands.

Ulcerative keratitis, hypopyon, iridocyclitis, and even panophthalmia have been observed. Sloughing of the glands may be so extensive that the large vessels lie exposed at the bottom of the ulcer. The walls of such arteries may become eroded and give rise to fatal hemorrhage.

The most important of all the complications is the septicopyæmia due to the concomitant micrococcal infection (Aoyama).

Among the more usual of the sequelæ may be mentioned the following: paresis of the vagus and of the recurrent nerves, aphonia, aphasia, amaurosis, deafness, and even paraplegia in exceptional cases. The deafness may in some cases be due to aural suppuration. Cases of periostitis have also been reported.

Pestis Siderans, Plague Septicæmia.

These are the peracute cases, characterized by extreme general disturbances and a comparative insignificance of the local lesions. The patient rapidly becomes comatose or delirious; uncontrollable vomiting sets in and later hæmatemesis, hæmaturia, evacuation of bloody stools, and convulsions mark the fatal termination, which may take place within a few hours after the onset or within a day or two at the latest. In these foudroyant cases death may occur before the glands are enlarged to any extent, but often tenderness over them may be elicited. At autopsy the glands as well as the periglandular tissue may be found œdematous and hemorrhagic.

It is important to bear in mind that in these cases the plague bacilli can be readily discovered in the blood of the patient.

Pneumonic Plague.

The onset in pneumonic plague is usually quite sudden and may resemble that of croupous pneumonia. There are, however, certain differences in the clinical picture. In plague pneumonia the dyspnœa is not so marked and there is no disturbance of the pulse-respiration ratio, which characterizes croupous pneumonia. Moreover, the pulmonary lesion is not lobar, but is lobular in nature, with corresponding difference in physical signs. The sputum may be serous, muco-purulent, or rusty brown, as it is in croupous pneumonia. The lymphatic ganglia are not notably enlarged, but tenderness may be elicited by pressure. The spleen is enlarged. Weakness and prostration are extremely marked, and out of proportion to the lesions discoverable. This form of the disease is usually fatal, and is said to be extremely contagious. This is perhaps due to the elimination of an enormous number of the specific microbes in the sputum. It may be added that the plague bacilli may be found in the sputum in these cases in pure culture, while in other cases they are associated with diplococci and streptococci.

The insignificance of the glandular changes in this, as well as in the foudroyant types of the disease has led some to question the pathognomonic importance of buboes in plague.

Course.

The foudroyant cases go on to a fatal termination within a day or two. In the majority of cases death takes place from the third to the eighth day (average the fourth day), but there are cases in which

it is delayed for a much longer period. In some of these cases the patient might be said to have died of marasmus or of some complication rather than from the attack of plague itself, as, for instance, when after a protracted course there is a gradual change indicating the supervention of pyæmic or septic infection, under which symptoms the patients eventually succumb. Death may also take place suddenly and unexpectedly. In such cases cardiac insufficiency may be assumed to be the cause, as for instance in cases in which a slight exertion has been followed by syncope and death.

Cases are reported in which death took place in consequence of hemorrhage from the eroded femoral artery consecutive to the sloughing of the glandular tumor. Severe hæmoptysis as an immediate cause of death has been recorded.

Pestis Minor.

Under the designation "pestis minor" are included various pathological conditions (all of favorable prognosis) presumed to be etiologically identical with the plague. In most of these cases, swelling of the glands is noted, or at least local tenderness, but with very slight general symptoms. There may be slight fever lasting for a day or two. Again, there are cases in which the glands are not affected in any way, and we note merely prostration, headache, vertigo, and gastrointestinal disturbances, but nothing to point to the relation of these symptoms to the plague. These cases are observed, however, during plague epidemics, especially in houses where there have been cases of plague, and the etiological identity is made probable by pronounced and disproportional prostration, and above all by the appearance of the sequelæ of the plague proper (German commission). So far as we know, a thorough bacteriological examination of these cases of so-called pestis minor has not been made. If these are really light cases of plague, they might be very instrumental in the propagation of the disease, a fact of great importance in considering prophylactic measures.

Diagnosis.

The clinical diagnosis of plague presents little difficulty, especially if the glandular swellings are marked from the outset. When the septicæmic form of the disease is suspected, a bacteriological examination of blood, or of the aspirated fluid from the glands, should be made. So also in pneumonic plague the bacilli should be sought for in the sputum. The initial vesicles or pustules, when they exist,

ought always to be subjected to careful bacteriological examination. We have already pointed out the necessity of a more definite diagnosis of the so-called "pestis minor."

The diseases which might come up for differentiation are typhoid fever, malarial fevers, glandular swellings of every description, dengue, and croupous pneumonia. The last has reference more especially to the pneumonic plague. With the exception of typhoid fever and pneumonia, the differential diagnosis should present very little difficulty; nevertheless cases are on record in which plague was diagnosed, and yet the autopsy showed widely different conditions—for example, influenza, as noted in the report of the German commission. Hysterical simulation has been authenticated in few cases. The importance of a bacteriological examination of blood drawn from the finger tip has been noted above in the section on bacteriology.

Prognosis.

The prognosis of plague is extremely unfavorable in the great majority of cases. Much depends naturally on the character of different epidemics and also on that of the disease at different periods of the same epidemic. Individually the intensity of the symptoms and presence or absence of the various complications must of course be taken into account. Septicæmic and pneumonic cases are almost invariably fatal. Even in light cases the imminence of heart failure must always be kept in mind. On the other hand, apparently desperate cases have, in exceptional instances, ended in recovery.

After convalescence the debility and neurasthenic condition may persist for a long time.

Morbidity and Mortality.

In no other disease is the figure of morbidity so large at the time of its prevalence as in this malady, as the histories of its pandemics show. In a given locality, too, the morbidity is extremely great; from one-half to three-quarters of the population has often fallen a prey to this pestilence.

The rate of mortality is also high—eighty to ninety per cent. may be given as the usual rate; in the Hong-Kong epidemic (1894), it was ninety-five per cent. The German Commission gives the plague mortality in Bombay (1896–97) as having been fifty to sixty per cent. It is to be understood, however, in looking for an explanation of this low figure, that the inclusion of the cases of pestis minor would make considerable difference in the mortality statistics.

Treatment.

The treatment of this malady has been mainly symptomatic and expectant. An initial administration of calomel has been found beneficial by some. Antipyretics have been administered, but with doubtful results, and of equally doubtful value is the injection of ergotin to control hemorrhage. Tepid sponging, often repeated, is very grateful to the patient and invigorating in effect. The strength of the patient must be kept up by nourishing diet, and extreme vigilance is necessary to guard against cardiac insufficiency. Alcoholic stimulants, ether, camphor, ammonia, and digitalis should be freely administered. Local treatment, such as the injection of a germicidal solution into the substance of the glands, has been tried, but with questionable benefit. Early incision and the application of unguentum cinereum have been recommended by many. Sloughing glands, especially if the large vessels be exposed, call for appropriate surgical interference.

Specific Treatment.

Since the discovery of the etiological microbe, attention has been directed to the possibility of orrhotherapy in this disease. Kitasato's laboratory experiments have been mentioned above, but his serum has not as yet been used in the treatment of plague. Yersin has also prepared a curative serum from his plague bacilli, and this serum has enjoyed extensive trial, particularly in Bombay. It appears that in some cases the results have been very encouraging, while other statistics again do not give so favorable a showing. The question of the efficacy of this serum therefore awaits further researches. It is obviously of primary importance to decide which one of the two distinct species of bacilli, Kitasato's or Yersin's, is to be regarded as the specific plague microbe, in order that we may establish the serum treatment on a scientific basis.

Prophylaxis.

In this section we propose to discuss briefly the mode of transmission of the plague virus in order to be in position to promulgate the requisite measures to prevent an outbreak, as well as those to be adopted in case of such outbreak, in order to extinguish the epidemic or at least to confine its ravages to the smallest limits.

We believe there can be no question concerning the direct contagiousness of this disease. In other words, we believe that the virus is

eliminated from the body of the patient, or found in the cadaver, in a state of virulence. The elimination takes place in the sputum (in the pneumonic form), in the urine, or in the dejections; and as the bacilli exist in the blood they may be found in the extravasated fluids or in any exudation whatsoever. After rupture or incision the exudation from the glands must constitute an exceedingly rich source of bacillary discharge.

The eliminated bacilli may find entrance directly or mediately into the healthy individual by way of inoculation (cutaneous infection), by inhalation, or by ingestion, as has been mentioned before. The port of entry in cases of cutaneous infection may be marked by local initial lesions, such as vesicles or pustules with lymphangitis. The case of Sticker is particularly interesting from the fact that the plague bacilli were found in the pustule on his finger. Usually the site of infection is not marked. It is presumed that a slight wound, a laceration or an excoriation, which has furnished the way for infection, may have healed over during the incubation period. That such is possible has been demonstrated by experimental infection of apes. They were inoculated by the puncture of a needle charged with the virus. The local lesions did not develop, but the infection was certain.

The record of intentional inoculation-experiments on human subjects is quite extensive. We will mention in this connection only a single instance of the kind, which is also one of the earliest, and seems authentic enough. It is the case of Dr. White (English army in Egypt, 1802), who inoculated himself by rubbing the contents of a bubo over the inguinal region, and on the next day again inoculated himself in the arm by introducing the virus under the skin. He died of plague, presumably in consequence of these inoculations.

The occurrence of pneumonic plague may point to infection by inhalation. Although the vitality of the microbe when desiccated is not preserved for any length of time—not to exceed seven days—still the German commission (working probably with Yersin's bacillus) has shown that the bacilli can live for a time in dirt and dust dry enough to be easily wafted into the atmosphere by slight currents of air. Then, again, there may be transportation of the virus in moist particles as has been shown to be possible by Flügge. The primary localization in the submaxillary lymphatic nodes, as well as the initial (?) ulceration on the tonsils, leads one to admit the possibility of buccal infection, but not necessarily infection by inhalation. Atkinson asserts the frequency of infection through ingestion. His argument is based on the fact that the characteristic changes are constantly found in the mesenteric and retroperitoneal glands, and at times, in these glands

exclusively; on the presence of the bacillus in the fæces; and lastly on the absence of the local lesions, which ought to be more common if the cutaneous infection was the principal mode of infection. We believe most of the reports hitherto published are not in accord with the above view.

As to the intermediary agents in the transmission of plague, we have very little concise knowledge. Personal effects and the various articles that have come into contact directly or indirectly with one suffering from the disease must be looked upon as contaminated. Flies and other insects may be the means of propagating the virus, and so also may be diseased rats and mice. Propagation of the plague by means of drinking-water has never been asserted as probable, and indeed the vitality of the plague bacilli in water seems to be of very short duration, not exceeding a day in ordinary drinking-water, and three days in the same water when it has been sterilized.

The relation of soil to this disease is very difficult to determine. It is possible that the bacilli may preserve their vitality in the ground for a certain length of time, and during such period they might gain entrance into the human system. As yet, however, nobody has been able to demonstrate the presence of virulent plague bacilli in the soil of infected localities, and it is certainly very hard to believe that the bacilli would be able to grow and multiply in the soil. It is conceivable that the microbes might exist in the soil as saprophytic microorganisms to acquire virulence at certain times, on the concurrence of necessary meteorologico-telluric influences. But it must be remembered that such a conception can be considered at present merely as an hypothesis entirely without scientific basis.

It does not lie in the domain of this monograph to enter into a discussion concerning the miasmatic theory of the infectious diseases. We might add, however, that all the so-called sanitary improvements of a locality, and especially of cities, are essential to maintain the health of a community, to prevent outbreaks of plague as well as of other epidemic diseases, and in a case of such outbreak to limit its progress, and make the prophylactic measures easier and more efficacious in their application.

Inspection, Isolation, Disinfection, etc.

In his preliminary report one of the present writers (Kitasato) expressed himself as follows:

"What means are to be employed against the plague? Preventive measures, general hygiene, good drainage, perfect water-supply, cleanliness in dwelling-houses and cleanliness in the streets. As

soon as an epidemic breaks out the sick must be carefully isolated. The infected dwellings must be disinfected, before the household things are removed, by a two-per-cent. carbolic-acid solution or by a solution of chloride of lime. Afterwards, wearing-apparel, linen, bedding, etc., should be specially disinfected in a steam disinfector for one hour at a temperature of 100° C.; should a steam disinfector not be available the things ought to be exposed directly to the sun's rays for several hours. Articles of little value ought to be burned. Dwelling-houses thus emptied should be cleaned over again with chloride of lime or carbolic acid. The fæces should be disinfected carefully with chloride of lime. The dead bodies covered with chloride of lime are either to be burned or to be buried at least three metres below the surface. Mice and rats which have died spontaneously in dwelling-houses should be carried away with proper precautions. After a patient has apparently recovered he must not be allowed to associate with the well for a period of at least a month, since during convalescence the bacilli may be discovered in the blood from three to four weeks after all symptoms have ceased."

Now as to isolation: in order to be efficacious, it must be carried out absolutely, and if it be imperfectly enforced, we are entitled to expect only a partial result. It is evident that in the present state of things, we are always obliged to content ourselves with the partial application, for the absolute realization is and will remain an impossibility. An early cognizance as to the evolution of the disease, which is the point of primary importance, is at all times difficult to obtain. Hence arises the necessity of enjoining compulsory notification, and also the necessity of medical inspection—house-to-house visitation. The fact reported by Kitasato that the microbes are found in the blood and the glands of the convalescent as late as three or four weeks after all the symptoms have subsided, makes the isolation of the convalescents necessary for the same length of time. We might add that for room-disinfection the applicability of Trélat's method should be borne in mind. It is to be noted that all these measures are attended with more or less expense; so that the thoroughness which is practicable in one place may be found impossible to be realized in other places. The attitude of the community as regards sanitary measures constitutes an important factor in the success of prophylaxis. Prejudice and ignorance may frustrate the best efforts of the health authorities.

The enforcement of a sanitary cordon is also very difficult of application in most cases, but the measure is an effectual one when enforced. All depends on the degree of thoroughness in each case. A certain amount of medical inspection with a view to the detention of

suspicious cases is certainly practicable in most cases. Quarantine may be enforced at the frontier; but it is doubtful if the requisite degree of thoroughness can be realized, if we take into consideration the immense obstacle it furnishes to international traffic and intercourse. The same holds true of maritime quarantine. Hence maritime powers like Great Britain have always protested against its strict enforcement. But on this point it is obvious that an international agreement should be arrived at in order to insure a successful and at the same time equitable system of quarantine. Thus by the initiative of the French government the first of the international conferences was held in Paris in 1851. The last of the series was held at Venice in 1897, and has special reference to the defence of Europe against the invasion of plague.

Specific Prophylaxis.

In order to lessen the morbidity as well as the mortality of plague, Haffkine has elaborated a specific method of preventive inoculation, quite similar to the Ferran-Haffkine anti-cholera inoculation. The "vaccine," or the material injected, is a virulent culture of the microbes, whose vitality, however, has been destroyed by heating the culture for thirty minutes at 70° C. The injections are made subcutaneously. The reports show quite encouraging results, but further investigations are desirable in order to obtain a confirmation of these results. The method of Lustig and Galeotti is a modification of Haffkine's. The vaccine is obtained by treating the culture with strong alkali and precipitating it by means of dilute hydrochloric acid. Yersin's serum is also said to possess prophylactic properties. The duration of the immunity produced by such inoculations is an important point which has not yet been satisfactorily determined.

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GLANDERS.

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GLANDERS.

Synonyms.—Malleus humidus; *Morve* (French), *Rotz* (German).

Definition.—Glanders is an endogenous, obligatory-parasitic, invasio-infectious disease, due to the pathogenic action of a specific bacillus within the body of a suitable host, which finds its historico-primary origin, and its present genesis invariably among the solipeds, principally the horse, from which it is extended to other animals and to man, directly or indirectly, but not to cattle and swine.

Etiology.

The scientific interest in a disease focuses on two series of conditions or factors: its etiological factors and their effects. It is generally the custom to write a special section on the history of a disease in an article like this, but as that history can only have to do with the ideas that have prevailed as to its causation, and the effects produced in the infested organism, it can be equally well considered in relation to etiology and pathological anatomy, and often with much better practical effect. The history of man is simply his endeavor to account for the existence and relations of conditions, himself included. The history of glanders is nothing more. While therapeutics should be based on an accurate knowledge of the two factors mentioned, it largely is not, but eventually it may become of more historical importance than at present. Prophylaxis is entirely based on such knowledge. As to glanders, while there is no therapeutics the prophylaxis is direct and simple. Death to the diseased covers the whole story.

As in all the endogenetic and probably in all the exogenetic diseases, we know nothing of the conditions which led to the primary origin of their respective parasites, nothing of the changes in environment which caused facultative parasites to become obligatory, and diseases once entirely exogenetic to become partially and then entirely endogenetic in character. We know nothing of the locality or time of primary origin. What we do know is the species in which endogenous diseases historically originate and to which their parasitic causes have become obligatory, much of their manner of extension, and much of the effects of parasitic invasion and infection within the infested

organism. No disease offers better opportunity to study these questions than glanders. The history of glanders is lost in the quicksands of tradition, or buried in the dungeons of ignorance. To Apsyrtus, a veterinarian in the army of the great Constantine, in the fourth century, is generally attributed the first literary mention of glanders, which he grouped with a number of diseases of like alarming character under the name of μάλις; but as Aristotle uses practically the same word for a group of similar diseases in the ass, though he distinctly says, "not of the horse," it is equally reasonable that glanders was included among them.

There can be little or no doubt that, as glanders is recognized to have existed in its present form four centuries after Christ, it equally well prevailed many centuries before. Proof of this can be drawn from the literature of the fourth and immediately succeeding centuries A.D. As to the ideas of these early writers in relation to the origin of glanders we are apparently in the dark, and find no fixed light until the appearance of a medical star of the first magnitude, for that time, Jordanus Rufus in the thirteenth century. In Rufus we meet with the first distinct mention of contagion as a positive factor in the causation of glanders, though he admits many other causes. The influence of Rufus was paramount all over enlightened Europe, and remained so for a long period, so that we need not be surprised to see the still more famous—as the author of the first equine anatomy and a treatise on the diseases of the horse —Carlo Ruini (fifteenth century), upholding the views of Rufus as to the contagious origin of glanders, though he also admitted the disease could arise out of many other conditions. But the most interesting and valuable work of this period is an encyclopedic compilation of Georg Simon Winter, or as he styled himself and is known in history, Winter von Adlers Flugel, entitled "Hippiater Expertus" (sixteenth century), in which is summed up all then known of the diseases of the horse and some other domestic animals; in fact so satisfied is the author with his work that in completing it he says: "This is all I know; if another knows more, let him write it."

Winter's description of glanders is far more exact than anything his predecessors have given us, and shows practical observation. He is a devout follower of Hippocrates and looks on the nasal discharge in glanders as a cerebral dyscrasia which cannot be checked or interfered with except with danger to the patient. He also explicitly tells us that "one horse can infect others," thus speaking for contagion as an active factor, though he permits many others to have equal force, some of which are most decidedly fanciful and amusing. Some time in the fifteenth century an idea arose common to the times, and still finding

believers among the laity, that glanders found its origin in the connection of syphilitic men with mares. The origin of this misconception has been traced to the outbreak of syphilis among the soldiers and glanders in the horses at the siege of Naples at that time. The same origin, with the change from mares to cows, has been given to bovine tuberculosis, and the habit of attributing everything evil to the French led the Germans to call this bovine malady the "Franzosenkrankheit," or French disease. This idea as to the connection between syphilis and glanders was taken up and spread abroad by the medical profession—Van Helmont (1682), and later by Ricord, the great syphilographer. Its absurdity is too great to merit further attention.

These historical notices have been given in order to show that from quite an early date contagion was considered to be an important factor in the etiology of glanders, though other factors were deemed of equal importance. Towards the end of the eighteenth century these ideas began to assume antagonistic positions in men's minds, with regard not only to glanders, but also to other infections, and we find a differentiation into two schools of thought becoming sharply though slowly demarcated; the one school being known as the Contagionists, with its motto, "No diseased horse no glanders"; the other, the De Novoists, or Nihilists, with their principle: Glanders can arise out of existing, without regard to any previous conditions—that is, something can come from nothing. The days of the fierce battles of the schools are over. The bitter hatreds engendered thereby are buried with the combatants, but the questions over which they fought, while in one measure settled, still face us, and will until the word contagiousness is not used for transmissibility, or else is used alone for that, which last is an impossibility on account of the classical use of the word in a primary genetic sense by the majority of medical writers and thinkers. Similar ideas to those prevailing on the Continent existed in England, but the contagionistic idea had still fewer and less positive advocates. In 1868 the most eminent authority on infectious animal diseases in England wrote that "the highest continental authorities, and those who have most attentively studied the etiology of glanders, are absolutely unanimous in the opinion of glanders being occasionally developed without contagion having anything to do with it;" and that "glanders appears among horses when unduly exposed, poorly fed, watered, etc., as in the army at times, or where hygienic measures are neglected and the laws of health ignored, or in large towns or establishments, if the horses are suddenly called upon to undergo severe exertion during bad weather and on an insufficient supply of food or forage of unsuitable character."

While these quotations fairly represent the feeling in England in 1868, and much later, still they are false and unfounded regarding the highest continental authorities. Gerlach, the highest of them all, had long since come out as a contagionist of the most pronounced type and bitterly opposed abiogenesis in any form, as did also the majority of the younger and leading men in Germany and Northern Europe. That glanders could be said to originate as described shows the utter inability of the majority of men, even professionals, to observe correctly and think for themselves. They could not differentiate between originating and extending conditions. The race has not advanced much in that direction. Englishmen had followed blindly in the wake of the abiogenetic nihilists of the Alfort school in France, whose influence cost that country an immense sum, and almost nullified the more correct teachings of the Lyons school, which finally prevailed to the benefit of all humanity. In spite of the fact that in 1868 the greatest English authority said that "the highest continental authorities" were de novoistic nihilists, and opposed to contagion as a genetic factor in glanders, nearly every veterinarian in France who made an historical record at that time was a pronounced contagionist, though he erred in giving too much genetic value to conditions which should only be appreciated as extension causes. In 1772 the great Lafosse wrote, "the primary causes of glanders are not known." Its contagiousness was clearly proven by Viborg in 1797. Thus we see that from the thirteenth century at least the weight of intelligent authority was on the side of contagion, though opposed by the inertia of ponderous ignorance in high places. So far as the Continent is concerned, the contagionists had won the battle "hands down" as far back as 1870, though it remained for the discovery of the specific bacillus by Löffler-Schütz, in 1882, to experimentally demonstrate the correctness of practical observation. The position of the contagionists over against that of the nihilists or de novoists, must be understood to be, *No diseased animal, no disease*, so far as contagious infections are concerned, thus justifying the position here taken of the classical historical use of the word contagious. This the contagionists held to as the primary and essential cause of glanders, utterly regardless of all other conditions, no matter how much apparent or claimed etiological value they may have had. The contagionists were able men who could distinguish between generating and extending conditions. They have not too many followers to-day. *No diseased animal, no disease* is the fundamental condition or law so far as endogenetic or obligatory-parasitic diseases go. It has the same value as *no bacillus, no disease*, for all bacillary parasitic diseases of both classes. It is even more fundamental in a

pathogenetic sense. *Noli me tangere* is the prophylactic law resulting from it.

The etiological factors in disease are generally spoken of as causa interna, causa externa, and causa sufficiens.

Causa Interna.

The causa interna may be termed the essential cause of contagious or obligatory-parasitic diseases. So far as pathogenesis goes, these causes are of equal importance in exogenetic or facultative parasitic diseases. It is the internal causes which properly constitute the contagiousness of a disease, for without them transmission of the disease is impossible, though the parasite itself may be easily transported from a diseased to a healthy or uncontaminated organism. If it is a law of infection, no parasite no infection; it is still more fundamental: No disposing conditions, no constitutional causes; that is, no suitable home, no proper food, no conformable temperature, no parasitic invasion, no infection. In other cases the animal organism may offer conditions suitable for the life of the parasite, but totally inadequate for its producing any toxic pathogenic material. Constitutional disposition, or conditions within the animal favorable to the life or pathogenity of the parasite, are the *sine qua non* to an invasive or infectious disease, whether endogenous or exogenous. Bacilli may be in all directions, the individual may be in a perfect hotbed of disease; the air may be full of pathogenic germs and the water may be swarming with them, but unless the exposed animal offer physiological conditions favorable to the life and pathogenity of the parasite, it is unaffected and seems "to carry a charmed life amidst death and devastation." We see this exemplified in cattle in relation to glanders, in thousands of people during epidemics of Asiatic cholera, in horses in relation to bovine tuberculosis and contagious pleuropneumonia, in all animals in regard to syphilis, and in most animals towards the majority of human parasitic diseases.

Artificial attempts to induce disease by inoculation of pure cultures of germs give ample proof of the total absence of the "contagious" constitution in many species of animal life in regard to the pathogenetic parasites of other species. The soil invaded is stony ground to the parasites. They fail to develop or they become harmless. Experimentalists, especially those of the Pasteur school, have taken more or less advantage of this internal condition to augment or mitigate the virulence of cultures taken originally from a species in which the parasite is naturally pathogenic. The fact that certain species of animals possessed constitutional indifference to certain diseases no-

tably fatal in others did not require the discovery of a microorganism, its cultivation, and inoculation of pure cultures into a humming bird, to demonstrate the non-contagiousness of the one species and the contagiousness of the other under suitable conditions to parasitic invasion. The internal causes then are the very basis of, the absolute necessity to parasitic invasion and disease, and the extension of the disease in animal life in any locality.

The Law of Parasitism and Infection.—No constitutional disposition, no physiological chemismus, on the part of an animal species, suitable to the life and pathogenesis of a given parasite, no disease; hence the source of primary origin, the species naturally the parasitic host, or the locality infested, is the first point of investigation, the fundament of pathogenic extension. The parasite itself is of secondary importance.

We hear and read much of the part "individual disposition" plays in the etiology and extension of parasitic diseases, especially as a means for explaining variations in severity in the course of a disease, or the apparent immunity of some and the varying susceptibility of other individuals of the same species. We also hear much of "predisposition." These two terms have most distinctly different meanings and should never be confounded. By disposition is meant that all the members of a certain species of animal life offer a suitable field for the pathogenetic life of a given parasite, unless something has occurred to disturb this condition in individuals. By predisposition is meant that certain individuals of a species have acquired certain weaknesses predisposing them to attacks from a certain parasite, a condition by no means common to the species under natural conditions. We can speak of predisposition in tuberculosis, but who ever heard of one horse being predisposed to glanders and another not. Disposition is invariably a chemical condition common to a species, while predisposition is as invariably an organic or constitutional weakness existing in individuals, sometimes common to families but never to a species.

Wherever variations exist in the susceptibility of individuals in a species in which a given disease is historically universal, or variations in the intensity of the disease in individuals, or at one time over another, the cause must not be sought so much in variations in disposition as in influences on the parasite from many causes during its life in the diseased animal or in the interval between its leaving the diseased and the invasion of another animal. Take glanders, for instance. Is there any doubt that if a sufficient amount of a virulent culture were suitably introduced in any number of horses that all would be affected? So pronounced is this fact in many cases of ex-

periment that one of the most competent investigators asserts that the infectiousness of a disease can only be determined in that manner, which is true as to race susceptibility but erroneously deceptive as to natural infection, to the prevention of which it is essential that we know all possible of the factors favoring and opposing its extension.

Acute and Chronic Glanders.

Among the most striking and interesting effects of the glanders bacilli in the infested organism is the idiosyncrasy in the course of the disease by which in some cases it is very acute and fatal in a few weeks, while in others it may extend over years, the animal being able to work all the time, though a source of danger to others. It is also worthy of note that the chronic form terminates in the acute when it ends fatally. Whether or not cure by natural limitation—self-cure—ever occurs in glanders is without satisfactory evidence.

The question that faces us is, What is the cause of this peculiar etiological idiosyncrasy in the clinical course of glanders? The easy answer is, Difference in the individual susceptibility to infection. But that is no answer at all. We do not know that such a condition exists. We do know that pathogenic microorganisms do vary in virulence, do lose their virulence entirely, even in a species naturally infected, and can often be made to lose or gain virulence by introduction into other species or by artificial means. When natural susceptibility exists in a species, we have not a particle of evidence that it lessens in one individual and not in another under the same conditions, provided they have never had the disease in question. It must be borne in mind that this racial or special disposition resides in the chemismus, organic or general, common to the individual organism of each and every member of the species and is not a personal or group characteristic. Variations of this character are most highly improbable. Some little experimental study of this question, while not positive, indicates that bacilli derived from very chronic cases of glanders are not so virulent when introduced into young healthy horses as those taken from fresh acute cases. Practical observation goes also to show that the more rapid the transmission of the disease from diseased to healthy animals in a large herd the more acute the disease, and *vice versa*. Is this due to variations in the natural chemismus of certain individuals or to bacillary conditions?

How shall we explain the transition of a long-time chronic case into a peracute and fatal one? Almost invariably this transition is connected with the interposition of acute constitutional disturbance, some other disease, or a surgical operation, whereby a general weakness of the animal is induced. The question is, Is this change in the

character of glanders then due to chemical changes in the equine organism by which the nutrition offered the bacilli causes them to become more toxic; or are tissue weaknesses alone produced which favor the overwhelming dispersion of the bacilli and greatly facilitate their multiplication? The weight of evidence is seemingly in favor of the latter hypothesis. One thing is sure. Under normal conditions there is no such thing as individual indisposition, or non-susceptibility to a disease idiopathic in a species in the sense of primary infection. All offer the same food and organismal conditions to the parasite.

Causa Externa.

Under the term external causes is embraced every factor external to or surrounding an undiseased individual liable to cause disease within it. In regard to parasitic diseases, this includes the host or individual infested by the parasites, the parasite itself, everything which tends to support the life of the parasite on its leaving a previously infested host, and every factor that acts, or can act, in the transmission of the pathogenic parasite from a previously infested host or an external locality of development, to the body of an uninfested individual. Leaving the inficiens or infestans, the parasite, entirely out of consideration, and treating it later as causa sufficiens, from a hygienic and prophylactic point of view, it must be seen that those physiological conditions of animal life which make invasion by parasites possible, and those external conditions in which they may live (exogenous parasites) and thrive, except when accidentally infesting (facultative) an animal organism, or those conditions which favor the life of an obligatory-parasite and its transmittal to a second host are of even more importance than the parasite itself. Without the knowledge of a single microorganism, and yet with the full conviction that a living something was the transmitted factor, living in one case external to the animal organism and only occasionally infesting it, and in another only in the organism of a given species and extending generally in that species only, our predecessors enunciated the infallible law of parasitic pathogenesis, that "while all contagious diseases are infectious, all infectious diseases are not contagious." An indifference to classical medicine—in part an offshoot of the spirit of the times, and in part due to a faddish regard for bacteriology and semi-deification of its leaders—has led to a neglect of the study of the history of disease which finds a base support in the so-called "practical tendencies" of the day, much to the injury of the profession and of a proper appreciation of the combatable factors in the etiology of para-

sitic diseases. In regard to glanders, it will be remembered that most authorities of the past were of the opinion that this pest could spring (like some pristine ghost) at one bound out of or into the equine organism under most conditions of treatment, feeding, and stabling. Nothing else was necessary. It was never thought that if such were the case the same conditions should produce the same effect in other animals exposed to them—cattle, dogs, or hogs, even men. Erroneous as this conclusion was, the hygienic results growing out of the consideration and removal of these suspected factors were not only of vast practical importance, but of such a nature as largely to support the conclusion of abiogenesis in the minds of those incapable of close observation and logical reasoning.

Law of Extension.—In relation to external causes and parasitic diseases the law of extension is: the closer susceptible animals are confined in the presence of an infested animal or locality, the more stagnant the circulation of the air, the more rapid the spread of the disease among the uninfested. Other conditions, bad food, no care, hard work, poor stabling, once supposed to be all-sufficient factors in the genesis of glanders, are but supporting causes, and incomparably of less importance than close confinement and stagnant air. Close confinement with poor ventilation will cause the most rapid extension of glanders, everything else being favorable to health in comparison to city conditions for the poorest class of horses. This is shown by some personal experiences among range horses in the West. If glanders gets in among them it will not extend perceptibly in a whole summer's free grazing, but when they are brought in and corralled or yarded for the winter, packing together to keep warm and frequently wounding each other, the extension of the disease will be very rapid and the fatality corresponding. Here we have everything favorable except the one factor of limitation of space; the animals still have the free heavens over them and abundance of room for exercise, but not for separation and isolated roaming. The prominent English authority previously quoted in favor of the spontanous generation of glanders, owing to unsuitable surrounding conditions and hard treatment, calls in proof of his position "the well-known extension of glanders among army horses in the late Franco-German and other wars"; but one of the greatest of German authorities writing of personal observations says: "When glanders occurs more frequently in times of war or mobilization of armies, the explanation is to be easily found in the fact that great numbers of horses are centred upon a small extent of territory and the opportunities to infection greatly increased thereby. This assertion is amply illustrated by a personal experience. In Prussia, where there is no want of mobilizing the forces, statistics

show that after such occasions glanders acquires a shocking extension among horses. The open nature of these manœuvres, as well as the known care and careful revision to which horses are subjected in the Prussian army, make it absolutely impossible that undue labor, bad feed, etc., should have any influence on these eruptions. In such manœuvres I once had occasion to review some one hundred horses that were turned loose into a riding place for the night and ran about among each other pell-mell. Of the one hundred seven had glanders. How many of the others, the further life of which I could not follow, could also have become infected? How different might be the conclusion of another who should examine the balance of those animals after the manœuvres? What cause could he surmise for their infection other than the vicissitudes of exercise unless he were a contagionist" (Leisering)? The most dangerous of the external causes of glanders to healthy horses as well as man is, first the diseased horse; second, the irresponsible dealer in such.

Causa Sufficiens.

"Nothing can come from nothing!" Though this truism was enunciated by Democritus twenty-five hundred years ago it has been very hard for the human race, inclusive of the medical profession, to comprehend it, especially in relation to pestiferous diseases. Difficult as it was for man in the past to appreciate the possibility of invisible parasites causing diseases, it is almost as difficult for modern medicine not to be run away with by the parasite and to appreciate, at its equal value, the fact that "no suitable host, no disease" is as fundamental a law as "no parasite no disease;" hence the term causa sufficiens is as applicable to the intra-organismal conditions, chemismus of the host, as the infesting parasite, though usage applies it to the parasite. While host and parasite are absolutely necessary to invasion, to infection two other factors are indispensable; one, that the parasite produces a toxic or pathogenic material, and the other that the host offers physiological conditions—nutrition—suitable to the parasite's needs in that direction. Therefore the actual specific cause in invasive diseases is the mechanical irritation of the proliferating parasite, while in infections it is the chemical result of the physiological life of the parasite in the infested organism. In other words, invasive pathogenesis is due to mechanical or physical irritation on the part of the infesting parasite; while infectious pathogenesis is due to the action of a chemical irritant as the product of parasitic life. This natural differentiation is being insisted on so strongly because, though general some twenty years ago, it is being lost sight of though erroneous tendencies in modern medi-

cine. With but two pathogenic factors in action, host and parasite, the disease would die out by natural limitation. Therefore external causes—the conditions supporting the ex-host life of the parasite, and favoring its passage from host to host, or locality to locality—the extension causes, are equally necessary to the completion of the pathogenesis of a parasitic disease.

Contagium Vivum.

There never has been a time when man did not believe in some vital force, some incarnation of maliferous energy, as an etiological factor in disease as well as in all the other ills human flesh is heir to. Devils and evil spirits entering into man and animals causing disease fill the records of mythology. Priest and physician were then identical. Exorcising and necromancy were the means of cure. According to this idea the devil entered into the afflicted. The same evil spirit afflicted all alike. There was truth in the idea. The chief error was the anthropomorphizing of the conception, and giving the devil a spiritual existence. An approach to a realistic conception of a contagium vivum began with the individualization and materialization of the suspected object, as something living in animals and passing from one to another, and, more important still, the belief that there was an independent something for the different pests, known to be such by the different deportment of the diseased. The first distinct conception of such an individualized entity is to be found in the "De Rei Rusticæ" of Varo and Columella, the great agricultural writers of the fourth century A.D. It is singular that it comes in connection with animal pests. The specialization of the infestans, or contagium, developed very slowly. It was often lost sight of in the chaotic pathogenesis of the nihilists. Still the truth had advocates, and the character of microetiological organisms, and much as to their manner of action, had been well inferred and men had been prepared for it (Henle) ere the final discovery was made.

Bacteriology.

The bacillus of glanders, bacillus mallei, bears some resemblance to that of tuberculosis morphologically, though chemically it is far differently constituted, not having the idiosyncratic affinity for certain dye-stuffs under special methods of treatment which makes the recognition of the bacillus of tuberculosis so easy a matter and of such inestimable value to the diagnostician. Bacillus mallei is present in varying numbers—the more recent and acute the lesions the greater the profusion—in all the diseased tissues and discharges of the infested

organism. It is a rod-like organism, appearing singly and in pairs, and occasionally in longer segments or threads, shorter and thicker than those of bacillus tuberculosis, with rounded ends; frequently the protoplasm is disintegrated and we have a beaded organism before us. Some have asserted the bacillus to be spore-bearing, but the little vital tenacity it has outside the animal organism, especially the quickness and completeness with which it yields to desiccation, and the little vitality it has in cultures, unless frequently changed to fresh media, all oppose such an assumption. While staining more or less readily in all the aniline dyes in laboratory use, it colors best in methylene blue added to a very weak solution of caustic potash (1 : 10,000). The bacilli do not retain color well, and if over-stained (necessary in sections) must be most delicately treated in decolorizing; a good solution for this purpose is: distilled water 10 c.c., sulphuric acid two drops, a five-per cent. solution of oxalic acid one drop. Expose the section for five seconds, wash in distilled water and xylol, and mount in xylol balsam. The bacilli have no motion and are aërobic, though it is claimed that they will develop in the absence of oxygen. They are as easily cultivated as any of the obligatory parasites growing (in the thermostat at 37° C.) fairly on most of the common media, such as glycerin-bouillon and glycerin-agar, on which they develop as a colorless transparent growth along the line of inoculation. It is said they will develop in room temperature on this medium. On glycerin-agar, made with milk instead of water, quite a marked growth appears in comparison with the aqueous material. Within the first two to three days the development of a pale-whitish coating takes place, which gradually changes in color, passing through an amber-yellow to a reddish-brown. But the most marked development of these bacilli occurs on the surface of potatoes, where it begins as a thinnish-yellow transparent coating—second or third day—having a resemblance to clarified honey; the transparency soon disappears and the amber color changes—sixth to eighth day—to a reddish-brown, the surrounding surface of the potato having an olive-yellow hue.

Modes of Infection.

By modes of infection is meant the ways and means by which the bacillus of glanders leaves the body of an infested and enters that of an uninfested host, and the ways and means of its preservation during the interval of passage from a primary to a secondary host: the causa externa. The substance or material which lodges pathogenic bacteria and by or with which they are thrown off from an infested organism, or in which they may live or thrive in their passage to another, is a virus. A virus may be said to be the medium for the preservation

and transmission of an inficiens. An artificial culture of germs is a virus. The nasal discharge, or that from a farcy bud, or the contents of an abscess, or a piece of infested tissue used for inoculation, is a virus. In the literature of the past, and many writings of the present day, the terms fixed and volatile are used in relation to the contagium, or infecting material. While the term "fixed contagium" has its value when used in its classical sense, that of volatile—by which was meant a gaseous material in itself infectious—has no meaning whatever. The term volatile was, however, an absolute necessity to the de novoists who insisted that an obligatory-parasitic disease could arise out of any evil conditions. A volatile substance, in the historic sense, while as a poisonous gas it might cause disease, has none of the characteristics of an inficiens and could never induce a transmittable disease. A volatile virus and a sporadic disease are twin terms conceived in the womb of ignorance in order to hide the abortive nature of the conception. That such terms were once necessary there is no question. A fixed virus is any material which confines the inficiens and with which it leaves the infested and enters the new host. A volatile virus, in a modern sense, is anything which holds the inficiens in suspension and with which it enters an uninfested organism but to which it is not attached—as the air. When an inficiens, like the tubercle or glanders bacillus, is passed off from an infested host in sputum or nasal discharge, the virus is fixed; if that virus be desiccated, and in that condition the bacilli are taken off as dust in the air and with the air aspired by an animal and infest it, the virus is volatile.

It is worthy of note that the first experimental demonstrator of contagion as a certain factor in the genesis of glanders, Viborg, and the first person unequivocally to deny abiogenesis or any other factor than contagion as the essential moment in the etiology of glanders, Gerlach, should both be quoted in evidence of the volatile property of the virus of glanders, which has thus far been either imperfectly appreciated or not at all recognized, and was first demonstrated about the end of the last century through the brilliant researches of Viborg (1797), whose observations were confirmed at a later date (1868) by Gerlach (Bollinger).

As the experiments alluded to, and those of Hertwig and Regnault, have occupied a very prominent position in the history of glanders and offer most valuable material to illustrate the points under discussion, it is well that we give them more detailed consideration. Bollinger continues: "Viborg and Gerlach succeeded in producing glanders in a number of horses by inoculating them with the condensed exhalations and sweat of glandered horses. . . . The nega-

tive results of the experiments of Hertwig and Regnault, by which healthy horses were made to breathe the expired air of glandered horses (by breathing into a canvas tube attached to the noses of each respectively), are to be attributed to the inferior degree of susceptibility of the animals on which the experiments were made, and do not argue against the volatile nature of the virus."

The discovery of the bacillus of glanders and the result of the studies of parasitic diseases of later years, while they contradict the assumption of a volatile virus in the historic sense, also show why the experiments of Viborg and Gerlach were positive and those of Hertwig and Regnault negative. Nothing else could have been expected according to our present knowledge. To attribute the failure of the Hertwig and Regnault experiment to the inferior degree of susceptibility of the animals used is an error. Under no form of natural exposure, no matter how apparently favorable the conditions, can we expect the uniformity in results sure to follow the inoculation of similar animals with pure cultures of virulent bacilli in sufficient quantities to insure infection. Very little was known of microorganisms then. Bacillus anthracis had been discovered and was thought to be a crystal or anything but what it was even by men deservedly high in authority. A bacillus in glanders was not even thought of. The experiments alluded to were valuable and still are. Those of Hertwig and Regnault beyond objection, those of Viborg and Gerlach all the more valuable because of the objections we are justified in raising against them. Gerlach says that only ten drops of the condensed fluid were used in his inoculation. Yet glanders resulted! Antibacillary precautions, as now practised in experimentation, were then unknown. There is no more doubt that bacillus malleus was in the material used by Viborg and Gerlach than that it could not be in the vaporous exhalations of a steaming-hot horse, if properly caught under modern precautions, or than that bacilli are not in the expired air of a horse diseased with glanders or of a human being with tuberculosis.

The experiments of Hertwig and Regnault are still more interesting from the fact that under the conditions of natural infection, glanders of the respiratory tract, particularly the lungs, is far more common than that of the nasal passages and cavities of the head, though the contrary is still often thought to be the case. Of two hundred and sixteen cases of glanders in which careful necroscopies were made the disease failed in the lungs in but ten, while it was wanting in thirty-three in the nasal cavities and sinuses of the head. Of the two hundred and sixteen cases the lesions in the lungs self-evidently antedated those in the nasal passages and sinuses in more than fifty per cent. These facts correspond with the necroscopical observations of every competent

observer. May not the assumption that the expired air of diseased horses is a volatile contagium and infectious be simply a conjecture founded on the known predominance of pulmonary glanders, and the logical suspicion that infection must have taken place by the aspiration of the bacilli, and that the air became polluted with them from the expired air of diseased animals? This assumption is often unfounded. In many cases in which glanders is acquired there is the utmost certainty that the secondarily infested animal has never been in contact with, or close enough to a diseased horse, or in a place where the latter had been so that it possibly could have breathed air directly polluted by the expirations of the diseased, and yet pulmonary complications resulted. The utter fallacy of infection by a volatile inficiens in the expired air must be self-evident when it is remembered that not only is the surface of the trachea and bronchial tubes moist, but that the mucous covering is so viscid as to hold anything like bacteria, when in normal condition. On the other hand, in diseased conditions of the lungs, such as glanders, tuberculosis, or pneumonia, bacilli-holding material can get into the air tubes and be carried to the larynx by the ciliated armament of the mucosa, passing out via the nasal passages, with no lesions in those passages in many cases; or this material may be swallowed.

How, then, are we to explain the great predominance of pulmonary glanders? As infection via the respiratory tract, that is, by aspiration of the bacilli, requires that the medium they are bound on becomes dry and they become mixed with other particles suspended in the air, we have to face the question of the inconsistency between pulmonary invasion and our experimental experiences with desiccated bacilli. Nasal discharge and scrapings from farcy buds replete in bacilli and very virulent when fresh, as shown by guinea-pig tests, attached to pellets of absorbent cotton placed in glass receivers and covered, and kept at room temperature, often lose their virulence entirely within forty days, as shown by the same tests. Such experiences, however, have only a suggestive value, as have those of direct sun drying or desiccation of cultures or polluted discharges in thin layers in the thermostat, in relation to the conditions of an infested stable with mangers and other things polluted by nasal discharges, etc. The general idea is, that under such conditions the bacilli may live and be virulent for months. As horses do not expectorate, and as under certain conditions of pulmonary glanders the bacilli may gain access to the air tubes and be wafted as sputum to the pharynx and swallowed, instead of being passed off by the nose, it is evident that the manure may be a vehicle of infection. All our laboratory experience points to the ease and rapidity with which these bacilli lose their virulence,

in ten days on desiccation, and in five days if suspended in distilled water. That the bacilli cannot pass the intact skin, when simply in contact with it, is shown by the experiences of those who have made autopsies; the writer has made over two hundred on glanders, and hundreds on fully as dangerous pests, and never thinks of using gloves, considering them dangerous snares. So far as glanders in man is concerned, all cases refer to infection directly by material from diseased horses, and yet nasal complication is still more rare than in horses.

As in tuberculosis the lungs invariably become complicated in the end, in every case of experimental inoculation that lasts long enough, so in glanders pulmonary complications will eventually result in every case of traumatic infection. It is well known that traumata do not need to be visible to insure infection. Local lesions do not seem the invariable necessity to local traumatic infection, or else cutaneous glanders would be far more common, in fact the prevalent complication. There is no doubt of a positive antagonism between laboratory experiences as to the tenacity and virulence of the bacilli and the conditions of infection as they occur in stables, etc., which requires detailed and exhaustive study. Volatile infection, by the aspiration of the expired air of a diseased horse, cannot occur. It must be remembered that it may not be necessary that nasal discharges and such stuff should be desiccated and turned to dust. Possibly they can give up bacilli to hay and other dust when not completely desiccated. With such material the bacilli may be lifted by the air and breathed in by healthy horses. The escape of man (grooms) and the frequently slow extension of the disease in a stable where such a horse may be kept, do not speak against aspiration invasion; but the possibilities of infection through cutaneous lesions seem to have the greatest weight of probability for the majority of cases, as the evidence now stands.

Incubation—Duration.

There is often a vast difference between the actual and the practicable. While the practical conception of incubation is the time elapsing from the moment of parasitic invasion to the first indication of their presence in the host by recognized general or local disturbances, the scientific idea should be that incubation begins with the moment of parasitic invasion and ends as soon as the parasites begin to manifest their presence in the tissues, whether such disturbances are outwardly recognizable or not. Every one of experience knows that in invasive diseases (chronic glanders, tuberculosis, actinomycosis, many animal and other parasitic disturbances), most severe and extensive tissue disturbances occur without the host's giving an

intimation of their existence, much less their extension over the organism. In infectious diseases the case is somewhat different, though the period of actual incubation is always somewhat shorter than the recognizable. It might be shorter than generally estimated, were more critical use of the thermometer practised. These errors are being slowly eradicated through the exactness of modern investigators.

Inoculation experiments in the naturally infested species can alone yield the desired information, and then only in case of acute action by active parasites in sufficient numbers. In acute inoculated glanders the period of incubation may be from four to six days; the duration of the disease from ten days to two or three weeks. In natural infection it is somewhat more protracted. In the chronic form, while there must be a period of incubation, it is undeterminable and the duration may extend months or even years. The longest term known to the writer, and then with no exact idea of the time of actual infection, is that of a horse which, without giving an outwardly suspicious sign of disease, was the cause of the extension of glanders in one stable for nine years and the loss of many thousands of dollars. The autopsy gave most widely extended pulmonary and other organic lesions of the most chronic type. In the text-books of medicine, we often read of a period of latency, which means the time the animal is diseased and not observed to be, and which is afterward found to have been a long time. Practically speaking, in chronic glanders there is no period of incubation, and the period of latency extends indefinitely. In glanders we labor under the difficulty that while chronic glanders invariably terminates in the acute, unless recovery by natural limitation occurs, the acute form seems never to assume a chronic type, so that in point of fact the period of incubation generally terminates with the eruption of the acute form in chronic glanders.

In this connection a very important and interesting question has been left open for discussion. The class of strictly invasive, that is, parasitic diseases, in which the parasites never produce any toxic or generally exciting irritant, has been frequently mentioned above; here they either act in a purely mechanical way, or what is more probable they produce or excrete a merely locally acting irritant which, while it excites the local cells to proliferation and causes neoplastic disturbances, produces no constitutional disturbance or infection. The one paradigmatic condition of an infectious disease, the one symptom, that of infection, has begun. The one symptom common to all infectious diseases is fever, as the result of a general disturbance of cellular activity, through a toxic stimulant produced by the parasite.

Fever is entirely wanting in invasive diseases so long as they re-

main strictly such and are not complicated by the presence of adventitious parasites. As in chronic glanders the period of invasion lasts from the time of the entrance of the parasites to that of the transition to the acute form, and the animals are free from fever during most or all of this period, not having even the periods of exacerbation and illness so characteristic of tuberculosis, does it not indicate that glanders may occupy an intermediate position and be a sort of invasio-infectious disease? In no other way can the entire failure to discover a definite period of incubation be explained. As farther evidence that chronic glanders cannot logically be classed as an infectious condition, and should be as a purely invasive one, may be mentioned the results of the mallein tests (in which the temperature is normal before the test) and the evidence of prolonged action of the bacilli at the necropsy. As noted in an early part of this treatise, what is the essential factor in the transition from chronic to acute glanders? Is it due to chemical changes in the chemismus of the host offering specific nutrition to the bacilli not before present, or to cellular changes favoring invasion and more rapid bacillary proliferation and tissue necrosis with absorption of a general irritant? Why this change from an invasive to an infectious condition in the same disease?

Bacillus Mallei in Action.

Having outlined the pathogenic factors in infectious diseases as exemplified by glanders, it remains to consider their further influence in and on the infested host. As has been shown, each species of parasite finds the conditions suitable to its life primarily in some special zoological species. Many require two or more localities, or hosts, of a different kind in order to complete their cycle of life. Bacillus mallei primarily infects solipeds, but may find a suitable host in other species. Trichinæ live primarily in swine and are obligatorily bound to them, but occasionally infest man and rats, and may infest any of the mammalia if properly introduced. The endoparasitic diseases of man are far more obligatory to him than those of animals. Not only does each species of parasitic life find its primary host in a special species of animal life, but the pathogenic parasites often find special tissues or organs more suitable to their biological necessities. Here the parasite lives, thrives, and "gets in its work." Here we study its effects. Here it sets up its types that we may, in a measure, read of its manner of life, and the message of fateful devastation it has prepared for us. A certain class of pathogenic microorganisms live in the blood of the host, and produce a toxic material which is carried by the blood over the organism, causing general irritation and disease. These are the septicæmic microorganisms. They may

also so multiply as to collect in the small arterioles and cause thrombosis or embolism with sequential local disturbances of the circulation and lesions in the complicated parts, phenomena well presented in glanders. Other pathogenic organisms remain at the *locus invasionis*, or point of entrance into the host, where sooner or later they multiply and replenish their kind (rabies, tetanus, Asiatic cholera), in addition to which they produce a toxic or pathogenic principle which is taken up by the lymphatics and transmitted to the blood—toxæmic diseases. These bacterial products again frequently exert their specific action on or in specific tissues, as in tetanus. Animal parasites are equally selective not only in the species they infest but in the tissues invaded of the individual host. Cœnurus cerebralis, as a tape-worm, infests the dog, while as a cysticercus it selects the brain and spinal cord of sheep, the embryo finding its way to these organs after the ova have hatched in the digestive tract of the sheep. Trichinæ find their way to the striated muscles of their host, after being born in the intestines, and may remain there as encysted embryos for years. Only such parasites as find these necessary hosts or conditions survive in the struggle for existence, and only those hosts which can withstand their attacks can be counted among the fit. Let us study bacillus mallei in its dynamitic effects in the organism of the hospitable equine and man.

As indicated several times the bacillus of glanders is doubly interesting from the rather complicated nature of its work in the organism of its host, being an invasio-infectious and not a simple infectious parasite. This point is really very important and worthy of serious consideration in the study of pathogenic parasites. Unless confirmed teleologists we are forced to the conclusion that what are now termed microorganisms, to speak more definitely, germs, pathogenic or saprophytic, represent the earliest living evolution of matter into life. Without going into the discussion of that point it suffices to say that germ life anticipated animal life by "milliards" of eons, and that all pathogenic germs must have been first exogenetic-facultative parasites; those that are endogenetic finally becoming obligatory because the conditions to their exogenetic life were no longer favorable, while the means for host transference had become more suitable to their survival in the struggle for existence. We have one pathogenic microorganism which illustrates this condition and is fast becoming as obligatory as it still is a facultative parasite. The way to overcome diphtheria is to render the exogenetic life of the bacillus impossible by hygienic measures. Its endogenetic life can then be easily taken care of.

Bacillus mallei presents two phases of evolution in its parasitic

life. In its invasive characteristics, in which it exerts a mechanical or local chemical influence on the surrounding tissue, and acts as a local proliferation-exciting irritant on these tissues, it may represent a form of atavism or retention of its earliest characteristic as a facultative parasite, while its infectious characteristics are an acquired attribute of its strictly endogenetic life; or it may have possessed both properties as a facultative parasite and retained them ever since. While many parasites are toxic-pathogenic, others are invasive-pathogenic to an equally exclusive degree. Still others occupy a middle ground, having both properties. The last are represented by bacillus malleus.

It now remains for us to consider the evidence in favor of this position. We must study the glanders bacillus *in situ* in its host. It has been shown that the bacillus can practically enter the host in but one of two ways, or possibly both in occasional instances; that is, via the respiratory tract or an abrasion or wound of the cutis. The only medium for its distribution over the infected organism from the locus or loci of invasion is the blood. This may be termed direct distribution. The bacilli, its products especially, may also be distributed from the point of local invasion by the lymphatics. Old terms that have fallen into disrepute often find their justification in the present, though we may not include all the honored fathers did under them. The general dyscrasia of Hippocrates is exactly represented by the septicæmias of modern medicine, while the local lesions are fitting examples of a local dyscrasia. The local lesions of glanders may be said to represent the Hippocratic local, while the toxæmia accompanying it in acute glanders represents the general dyscrasia. Humoral pathology finds its justification in both toxæmias and septicæmias.

Long before the discovery of bacillus mallei it had been experimentally demonstrated that the blood contained something that was the cause of glanders. What that something was no one knew.

Schimming (Dorpat, 1875) sums up the results of these experiments as follows: "Venous blood from a glandered horse injected into the veins of a healthy one will induce glanders." "The quantity of injected blood appears to exert an influence upon the duration of the incubatory stage," which simply means the incubatory stage is or may be quantitatively determined by the bacilli in the blood injected. "The blood from a glandered horse appears to have less intensive action in healthy animals than the nasal discharge or the secretion of a farcy bud"—a clever observation explained by the blood containing far less bacilli.

These and many other facts over which our predecessors theorized

and built hypotheses have found their explanation in the discovery of the bacillus. Theory is but a mass of hypothetical links which we endeavor to forge into their places in the chain of sequence to make it complete. That is science!

The specific pathogenic products of bacillus mallei are still unknown. The material called "mallein" is a thing *per se* in name only. How much it is a product of the bacilli and how much the result of the decomposition of dead germs is uncertain. We are told by Vaughan (Vol. XIII. of this encyclopedia, page 109) that one of the "preparations—termed mallein—contains numerous substances, peptones, globulins, xanthin, guanin, tyrosin, leucin." As all mallein preparations are made in about the same way they must closely resemble each other. In proof that the material called mallein does not represent the essential pathogenic or toxic factor of bacillus malleus, it is only necessary to note that the injection of healthy horses is not followed by serious disturbance. Why, then, should we be told that "the toxin of glanders is mallein and contained in the bacterial cell," especially when we are told that "it has been shown that there is nothing specific in this action of mallein (the so-called diagnostic action), inasmuch as the same effect is produced in glandered horses by the injection of toxins obtained from other bacteria." If the position here taken as to the action of the bacilli of glanders in its host is correct, then it will be found impossible to prove the discovery of a or the toxin of glanders, if the proof be that required of the bacillus, the reproduction of the disease *in toto* by the inoculation of pure cultures, the same as occurs in natural transmission. This assertion is equally true of syphilis, tuberculosis, and every parasitic disease characterized by neoplastic products. The neoplastic products represent the invasive nature of the parasite; the fever and parenchymatous changes either its toxic action, that of adventitious germs accompanying its invasion, or the necrobiosis of the neoplastic and invaded tissue and the absorption or generalization of the product over the system. The general disturbances and the local neoplastic phenomena can never be the result of one and the same cause unless we go to the bacteria as such. The neoplastic condition must either be the result of the local development of the microorganisms or of a germ product which acts only as local tissue irritant, for in glanders as in tuberculosis and syphilis the neoplastic processes are constantly going on in periods when the host is absolutely free from fever, the only pathognomonic phenomenon of infection. Infection is general. It can never be local except in origin. In so far, then, as the glanders bacilli are neoplastic in their action, in so far is the disease invasive.

Although none of the chemical products of bacillus malleus are known to us, the results of the presence of the bacilli in the host force the assumption of at least two distinct chemical products, each having specific action. With the general toxic or fever-generating product we have little or nothing to do. Infinitely more important as are its effects, being in fact the fateful product of the parasite in relation to its host, still they are so well known and common to so many diseases that they need no detailed discussion. Its action is manifest in fever, diffuse parenchymatous changes, and their effects on the general condition of the host. These lesions and the rise in temperature in the acute form of glanders find their cause entirely in a specific toxic product of bacillus mallei. A certain part (how much is not known) of these disturbances is undoubtedly due to the action of adventitious microorganisms, when present, which gain entrance at the superficial lesions of the specific bacilli, and often accompany them in their dispersion over the body. Another portion of these disturbances must be attributed to the irritating action of the necrobiotic chemical products on the cell action in general. It is evident, therefore, that the action of a specific "mallein" in glanders is more or less limited even in the acute form and quite questionable in the chronic.

As heretofore noted every pathogenic microorganism has not only its peculiar zoological host, but its peculiar tissue or organ in which it lives and upon which it exerts its effects. Added to this the infectious parasites often exert their influence on special tissues or organs through a specific product. Whether this product is invariably the direct cause of the general disturbances is questionable. In tetanus, for instance, the specific action of the toxin is on the motor neurons in the cord, and it is a question if the fever and some at least of the parenchymatous changes in other organs than the muscles are not of secondary nature and largely reflex.

The one effect of bacillus mallei which can be surely attributed to a chemical product, a toxin, is a diffuse irritation of the connective tissue of the body, manifest in the dense parenchymatous organs when it becomes more or less sclerotic. This diffuse irritation of the connective tissue has no relation to the common neoplastic products, tubercles, nodules, nodes, and irregular growths, to which has been given the name granulomata from their relation to granulation tissue. These neoplasms have an entirely different primary origin. Naturally this diffuse complication of the stromatous connective tissue can only occur in the chronic form of glanders. As fever is seldom present in this form it is evident that the same toxin which causes fever cannot be the cause of this diffuse irritation of the connective tissue. This

disturbance is to be seen in the diffusely shrunken kidney of chronic glanders, the disturbance being manifest in life by albuminuria and often also by casts in the urine. In the liver the same shrunken condition is to be seen, which is also manifested in the brown atrophy of the liver in chronic glanders. The dense, hard, unelastic condition of the spleen must also have been noticed. The lymphatic system, particularly the glands, undergoes the same disturbance. Induration of the peribronchiolic and arteriolic tissue comes in the same category.

The Neoplasmata.

The circumscribed neoplasmata in glanders have a far more direct or immediate relation to the bacilli than the diffuse sclerosis of the stromatous connective tissue just spoken of. The question is, How far direct physical irritation of a circumscribed colony of bacilli takes part in their production, or how far it is due to a chemical irritant, the product of the colonized bacilli. The direct origin of these neoplasmata must be sought in the bacilli in the first place, and their direct irritating action on the tissue immediately surrounding them. The bacilli are carried over the body from the primary seats of invasion directly by the blood circulation, aided indirectly perhaps by the lymphatics, through which they may finally enter the circulation. Other neoplasmata find their origin in the action of bacilli within the bronchioles or at their bifurcations. At present we have to do with the distribution of the bacilli by the circulation, which we will consider under the head of

Direct and Indirect Metastasis.

The blood-vessels may be termed the canals for the dispersion of invading parasites over the organism of the host, while the blood itself may be looked upon as the dispenser of their fruit.

One of the favorite theories of some of the writers on glanders in the first half of this century, or even later, was that it was a pyæmia. The assertion has been denied by many, but it cannot be successfully contradicted, if we limit its bearing to the so-called neoplasmata. The question is, What do we understand by pyæmia? If the historian of medicine is consulted, he tells us that from some local abscess or purulent centre pus gets into the blood and is carried *as pus* over the body, and left here and there at convenient places where it causes new or secondary pus centres or abscesses. In this historical sense, then, pyæmia is pus or abscess metastasis via the blood. Instead of pus metastasis we now say that pyæmia is the conveyance by the blood current of pus generators from their seat of primary action in the body to secondary localities where they develop and generate pus

centres similar to the first. A great difference in point of fact, but none in the essential idea. It is evident that pyæmia in the modern sense does play no inconsiderable rôle in glanders. Leukæmia is quite a common condition in chronic glanders, and the fact that abscess formation or pus generation to a widely dispersed degree is quite common justifies the conclusion that the ancient physicians, seeing both, thought the leukæmic blood came from a local abscess by absorption and formed new ones by deposition. Metastasis is the larger and more general name which includes pyæmia. Metastasis plays a big part in the development of neoplasmata in glanders. Bacterial embolism is the chief factor. If the emboli consist of bacilli mallei, pure and undefiled, simple uncontaminated neoplasms may result. If adventitious, pus-generating germs are mixed up with the glanders bacilli in a primary lesion, and the germ mixture gains access to the circulating blood, forming bacillary emboli, then the secondary processes are no more benign neoplasmata like the first, but are malignant, degenerating, purulent, ichorous—in other words, pyæmic. The question is, Are the glanders bacilli pus-generators when virulent?

Glanders being invariably due to local invasion, in the first instance, let the locality be in the nasal passages, the larynx, trachea, lungs, or skin, the pathological disturbances do not extend to any great degree *per continuitatem*, that is, by the direct and gradual invasion of the tissues surrounding the *locus invasionis*, but in one or two ways which may be called direct and indirect blood transmission or metastasis.

By *direct metastasis* is meant the immediate entrance of the bacilli into the veins at the seat of invasion by corrosion of their walls, and the transference of the bacilli over the body by the circulation until they collect or lodge in a small artery or arteriole, bacterial embolism, forming an embolic infarct, which may be benign or malignant in accordance with the virulence of the glanders bacilli or the admixture of pus-generating germs. The chief seats of such bacillary embolic infarctions are the lungs, the respiratory mucosa, including that of the nose, and the skin or subcutis, any of which localities may also be the seat of the centres of primary invasion. As these localities of primary invasion are invariably more or less directly in contact with the open air, especially the nasal mucosa and the skin, they offer the very best opportunity for the invasion of the common pus-generating with the specific germs. In case of bacterial embolism from such centres, the infarction is sure to be malignant and the resulting neoplastic products of a necrobiotic nature, from which again bacillary embolism to other parts may take place. It has long been known

that thrombus formations in the veins in the nasal septum or in the subcutis in the vicinity of the necrobiotic lesions of acute glanders are very common, and as the necrobiotic processes extend to the walls of the veins the thrombus must undergo putrid degeneration, and the emboli from it must have the same characteristics, and such characteristics must extend to neoplasms due to these emboli or infarction processes.

It has been claimed that a certain proportion of the neoplasms in glanders, especially the tubercles, were invariably developed around a central vessel from which radiated a network of capillaries, between which were cells. The same is also true of a certain portion of the nodes as well as larger growths; that is, they extend from the walls of a blood-vessel. When the emboli are composed entirely of bacilli mallei, pearly, hard, enduring tubercles or growths develop; when other germs are mixed with the glanders bacilli necrobiosis begins in the centre or in the immediate vicinity of the vessel. Whether this interpretation be correct or not and whether or not the bacillus malleus is pus-producing in virulent form, the conditions described may be seen in every comparison of chronic and acute glanders. As has been previously intimated, if on the mallein test being applied to a case of suspected chronic glanders the reactive fever occurs, and we know that for months previous the animal has been fever free, and on a necroscopical examination we find simply indurative sclerotic neoplasms and only glanders bacilli, with a tendency to calcification rather than dissolution, and on the necroscopy of a feverish, acute case find ulcerations in the respiratory tract, softened thrombi in the veins and necrobiotic neoplasms and infarctions full of mixed germs in the lungs, what are we to think? Are we to assume that the glanders bacilli form a fever-producing, tissue-destroying toxin which is dispersed over the body, or that in reality the toxin is the product of adventitious germs? Certainly, the conditions indicate the last to be the case. It is certain that the fever-producing substance is immediately connected with the necrobiotic conditions of acute glanders, as fever is not an accompaniment of chronic glanders; and, as the microorganisms in the fresh tubercles and nodes of chronic glanders are most generally bacillus malleus only, and no fever is present, to what conclusion are we forced? To be sure, variation in virulence may account for the differences in acute and chronic glanders, adventitious germs only aiding and abetting in the acute form.

Indirect metastasis, or the indirect dispersion of the bacilli from the seat of a primary lesion, takes place by the lymphatics, as well as do the absorption and dispersion of any chemical products of the germ in the infested centre, or of the necrobiosis of tissues in such

centres From the lymphatics such factors are poured into the blood, and from thence metastasis to other organs takes place, or the chemical irritants are distributed over the organism of the host. When bacilli find their way into the lymphatics and become fast in the tissues of the next lymph glands, the resulting neoplasm will exactly resemble those mentioned above. If the bacilli are strictly those of glanders and not very virulent, benign neoplasms subject to sclerosis or calcification will be formed; if the bacilli are virulent or other germs are mixed with the glanders bacilli, necrobiosis, pus formation, and an abscess are sure to occur in the gland. An abscess in the lymph glands is evidence of pyæmia or the extension of pus-generators from an ulceration in the territory drained by the lymphatics leading to such a gland.

Respiratory Infection.—Infection via the respiratory passages, that is by aspiration of the bacilli, is generally thought to be the most common way of infection in glanders. While this may be true, it by no means bars the fact that metastatic lesions in the lungs may occur in a case of cutaneous or nasal glanders as the primary lesion. It is also a fact that metastases from a malignant case of farcy may have a like character in the lungs, and that from the pulmonary lesions metastases to the bronchial, tracheal, and nasal mucosa may take place, which will have the character of the original lesion. On the other hand if infection per aspired bacilli takes place, the glanders bacilli must have the ability to attach themselves to the mucosa, and either penetrate the intact mucosa or, what is more probable, begin their work by invading the neck of a mucous gland, where they multiply and still further invade the tissues. The fact of atelectasis being a common lesion in the lungs in glanders does not necessarily point to the entrance of the specific bacilli into the bronchioles, for that condition may follow any catarrhal obstruction of the bronchioles. On the other hand, the extension of large neoplastic indurations from the walls of a bronchiole, the character of the lesion often giving rise to the most extensive developments of this kind, points to the inhalation of glanders bacilli.

The absence of lesions in the intestines indicates, or makes improbable, that infection does not occur that way, even though it is true that glanders bacilli must be advanced to the pharynx, both in nasal and in laryngeal, tracheal, or pulmonary glanders, and must of necessity be swallowed. If not destroyed in the intestines of the host, as the absence of intestinal lesions most strongly indicates, the bacilli must be passed off with the fæces which in this way may play a serious part in the extension of the disease, and which must be suspected until the contrary is in some way proven.

Pathological Anatomy.

Having in the previous section endeavored to indicate the work of the bacilli in the infected organism and the genesis of the principal lesions, it now becomes us to consider the latter in an objective sense. The characteristic lesions in glanders consist in a more or less scattered development of tubercles or nodules, nodes, and irregularly shaped neoplasms of more extended dimensions. In acute glanders the general tendency is to the development of neoplastic, necrobiotic processes which pass at once into ulceration and abscess formation, and a widely disseminated tuberculosis. In chronic glanders the tendency is to the development of similar neoplasms, with the addition of extensive neoplastic indurations which have the characteristic of permanency much more strongly marked. In the discussions, some twenty years since, of the lesions of glanders as well as those of tuberculosis and all neoplastic processes men wore themselves out in the endeavor to discover and defend the individuality of specific cells, and the literature is full of polemics as to what was or was not a specific cell. We may read learned discussions, of once great authority, of the specific diagnostic points of glanders cells, tubercle cells, cancer cells, etc., and that giant cells were pathognomonic to tuberculosis, all of which has now been shelved among the antiquated "curios" of traditional pathology. Tradition is invariably attached to error. History purges it of error and then it becomes fact instead of tradition. The result of pathogenetic investigation, since the introduction of microorganisms into the arena, has been to disband the deceptive array of specific cells, and the recognition of the fact that all neoplastic cells are but the same thing as the embryonal form of the matricial tissue in active development, often modified into abnormalities, but still recognized as occurring somewhere in normal development. If there is anything morphologically specific in a neoplasm it is the variation in the reciprocal relations or a disarrangement of the cells from the normal type of the tissue from which they spring. Neoplastic osseous tissue may be bony or osteoid, but it can never have the regular arrangement of physiologically developed bone. The neoplasms of parasitic generation find their specificity not in their cell structure, but in the presence of their specific cause. Given two pieces of lung tissue of equally fresh nodular or tubercular eruption, with no history, upon the same species, the one of glanders, the other tuberculosis, the differential diagnosis would depend on the demonstration of bacillus tuberculosis far more than on differentiation in the cell structure, which

no sensible pathologist would bother about to-day. In this regard not many years have passed since a board of health condemned an immense number of sheep carcasses on account of tuberculosis, the lungs being fairly filled with disseminated tubercles and pneumonic centres. While tuberculosis may or may not be limited to phthisis tuberculosis, there are many varieties of tuberculosis verminosa equally specific. That in the sheep's lungs was of that nature. These tubercles never undergo caseous degeneration, never form conglomerations, never form cavities. They do calcify. In every fresh one an embryo worm may be found. Barring the worm, in a cellular sense they could scarcely be differentiated from a very fresh glanders or specific phthisical tubercle. They, too, are composed of round but very few migratory cells. They are a fibrous variety. There are others. It is only limitedly true that "the neoplasms in glanders, the granulomata, are but the accumulation of migrated leucocytes." It is true that the very transient neoplasms, especially tubercles, of acute, and the more slowly necrobiotic of subacute glanders are composed of those cells, but the slower the development of the neoplasm the more is its structure made up by the round cells of connective-tissue proliferation and the more permanent is the tissue, it having more strongly the tendency to organization. While there is no doubt that the permanency of the neoplasm is dependent to a large degree on the various stages of virulence of the etiological bacilli, it is no less true that the nature of the matricial tissue plays an important determining rôle. There is far greater tendency to permanency in the tubercles or circumscribed neoplasms in the lungs or the lymph glands than in those in the mucosæ or cutis, and more still than in those in the liver and spleen.

Too much stress has been laid on the bacilli alone in this regard, and also in the assertion that it is due to the bacilli entirely that the tubercles in phthisis are more prone to conglomerate development and caseation than they are in glanders, whereas the nature of the tissue invaded more largely determines that point; the bacilli in tuberculous phthisis developing in a vitiated and predisposed tissue, while bacillus malleus comes in contact with a healthy tissue and the physiological disposition, at least in the horse, facts which cannot be overlooked in considering results in parasitic invasion.

In glanders, at least, the differentiation of its clinical course into acute and chronic has far more to do with the explosive toxic infection than the local lesion *per se*, which acts principally as the doorway of direct infection.

Lesions in the Nose.

It has been generally the custom to differentiate the consideration of the lesions in glanders as nasal, pulmonary, and cutaneous glanders, to which there would be no objection were it not that such marked individualization has a bad effect on the mind of the inexperienced reader, in whom there is always too much of a tendency in that direction. This specialization of lesions is one of the weaknesses of modern pathology. On top of that the error has a strong traditional foundation and is fast rooted in the mind of the laity and many practitioners. Its generalization may be traced back to the great Lafosse, who speaks thus disdainfully of his predecessors and their opinions: "The ancient authors knew nothing more of the seat of glanders than they did of its treatment. Some looked upon it as located in the head, others in the lungs, others in the kidneys, others in the stomach, to all of which they gave the name of glanders."

That Lafosse knew little more than those "ancient authors" he at once shows in asserting that "to assume that glanders is seated in the lungs is pardonable: (1) because they communicate with the nose; (2) because a discharge from the lungs by way of the nose does take place; (3) because it is often mixed with the nasal discharge." . . . "The ancient authors often erred in distinction. To assert that glanders is situated in the kidneys, spleen, liver, or in the brain, is contrary to good sense. They utterly ignored the fact that there was no connection between those parts and the nose" (*sic!*).

"I distinguish glanders according to its nature, as glanders properly speaking, and glanders improperly so called.

"True glanders is the discharge which comes alone from the pituitary membrane of the nose. It is improper to speak of any other form of glanders than this. Every other disease than this is not glanders.

"Glanders may be distinguished as simple and complex. Simple glanders comes from the pituitary membrane direct. Complex glanders comes from the same and the lungs at the same time. Primitive glanders comes independent of all other complications. Secondary glanders is that which follows on other diseases."

Great as was the authority of Lafosse he was ignorant of the facts. It would seem as if an author who could write thus had never made necroscopical studies in a case of chronic glanders. Such is probably the fact, for "pulmonary" glanders did not become known until a half century or more after Lafosse. The idea of Lafosse prevails

in the world still. It is very difficult to make a horseman believe an animal has glanders when free from nasal disease.

It will be remembered that of 216 necroscopies on horses killed on account of glanders, lesions were found in the lungs in all but 10, and were wanting in the nasal cavity in 33. Of 52 other necroscopies the lungs were found intact in but 4 and the nasal passages in 5; the larynx, trachea, and bronchi were diseased in 12 of these 52, and in 7 of the other 11 examined. Pulmonary lesions frequently antedate those in the nasal passages. In the 216 before mentioned, this was the case in more than half. If the nasal mucosa is as much the seat of bacillary invasion in glanders as the genital organs in syphilis, surely the "footprint on the sands" is wanting.

When the primary invasion of the nasal mucosa is from or by bacilli in the aspired air the lesions are superficial and generally extend in the same manner. On the contrary, if the nasal lesions find their origin in the blood circulation and bacillary embolism, while they may be equally extensive they will also generally be far more profound in their effects. In either case the first disturbance of the mucosa will be a disturbance of the circulation and diffuse hyperæmia darker in the centre. In this hyperæmia will be seen a circumscribed, gradually becoming opaque centre, varying in size from a small pinhead to that of a millet seed. These neoplasms are often isolated; again they appear in groups, never in the conglomerates of tuberculosis proper. The structure of these tubercles has been already discussed. When the result of very virulent germs and in acute or subacute glanders they are composed entirely of migrated leucocytes and at once commence to break down. In this way small ulcers are formed which soon coalesce, thus forming ulcerated surfaces with ragged edges and irregular confines which extend in

FIG. 1.—Extensive Ulcers of the Mucous Membrane of the Nasal Cavity in a Horse. The base of the ulcer is corroded and the edges are everted and studded with tubercular growths. Near the lower edge are some small ulcers of more recent formation, with tubercles in process of being transformed into ulcers (Bollinger).

circumference by the development and necrobiosis of similar tubercles in the tumefied edges, while they extend in the same way in the tissues at their base which is covered by a more or less viscid, grayish-white, yellowish-white, or reddish coating composed of round cells, exudate, and sometimes extravasations. The uncomplicated tissue between and around these ulcerations is intensely swollen and hyperæmic in their immediate vicinity, gradually becoming less so as they are departed from.

In the subacute and chronic forms the stroma or connective tissue of the mucosa and submucosa comes into action and proliferates, the cells going into the structure of the neoplasm, which has more permanency of character. It is here that the great cicatricial deformations of the mucosa, which sometimes twist the septum nasi out of shape and position, largely find their origin. So great and widespread is this cicatrization and so wonderful are its radiations, that it has been happily compared by Rabe to the frost pictures on our window panes in winter.

FIG. 2.—Indurated Cicatrices of Former Ulcers on the Mucous Membrane Covering the Septum Nasi in the Horse. These parts present a white, glistening appearance, and are but meagrely supplied with blood-vessels. Below are seen fresh ulcers of a more recent crop (Bollinger).

The necrobiosis often extends to the tissues of the septum nasi in that form of nasal invasion connected with chronic glanders which is due to bacillary embolism in the arteries of the septum. The necrobiosis is so extreme in such cases that penetration of the septum takes place and irregularly shaped holes are made. In others less severe the deformation may be so extreme as almost to occlude the passage into which it is deflected.

It often happens that an animal may have had a primary affection of the mucosa of the nose which healed, leaving cicatrices behind.

Nothing suspicious is to be seen unless on most exact examination with the aid of a reflecting speculum. The animal may remain in this condition a long time, the processes going on in the lungs and other parts, when suddenly nasal complications will appear. In such cases they are invariably of embolic origin. Ulcerations may develop in the cicatrized tissues if they happen to have arteries of sufficient dimensions running through them. Probably from incomplete embolism a disturbance of the mucosa sometimes occurs, to which the name of diffuse infiltration may be given; the tissues become swollen and hyperæmic, proliferate, and form irregularly contoured "scales" of induration in the mucosa, closely attached to underlying tissues. In the immediate vicinity tubercles often develop, accompanied by ulceration.

FIG. 3.—An Elongated Cicatricial Band, with Lateral Projections, in the Mucous Membrane of the Septum Nasi, in a Horse with Chronic Glanders. On the left is seen an isolated ulcer, also in process of cicatrization (Bollinger).

As mentioned in previous pages, the necrobiotic complications of the mucosa, which are generally situated in the upper half of the passages, often extend to the veins and attack their walls, causing thrombus formation. At other times the extension is so rapid that incomplete thrombosis takes place, and erosion of the wall occurs accompanied by hemorrhage; the thrombi are then soft and contain not only the specific bacilli but other germs. It is in such cases that so much malignant embolism and metastasis occur. Similar lesions, though more of the isolated tubercular nature, occur in the sinuses and on the conchæ.

LESIONS IN THE LARYNX, TRACHEA, AND BRONCHI.

The mucosa of the trachea is complicated in almost the same way as that of the septum nasi, though it is doubted by some authors if it ever occurs from bacilli in the inspired air. This is far more probable than the assumption of insufflation of bacillary material from the lesions in the nasal cavity. The most probable causes are that the

bacilli are in the air, or bacillary material comes to the trachea and larynx from lesions in the bronchi, which may be caused by aspired bacilli or from the lungs proper, which may have the same or embolic origin. Lesions of the trachea or larynx may be found in from fifty to sixty per cent. of the cases of glanders necroscopically examined. They are very common in the Morgagni diverticles in the larynx, less so in the introitus laryngis and on the epiglottis. Cicatricial formation in the anterior wall of the trachea is often excessive, the extensive oblong ulcerations extending between the rings and complicating the peritracheal tissues. In one case the deformation in the course of the trachea could not only be felt externally, but could be distinctly seen; on autopsy fibrous shreds like wires ran across the lumen of the trachea. This horse was not suspected of having glanders by the owner, there being no nasal discharge, but was brought for examination on account of "its wind." The lesions in the finer bronchi are generally tubercular, ulcerative, and not so extensive as in the trachea. Obstruction of the bronchioles and finer bronchi with catarrhal secretion is very common in chronic glanders, leading to the development of cylindrical ectases of variable dimensions that are filled with a thick, creamy, purulent material. These ectases have been frequently mistaken for abscesses.

Glanders in the Lungs.

Notwithstanding the intense interest which glanders has awakened and the amount of earnest thought and intelligent investigation that has been given to it, and in the face of the practically unlimited amount of material for necroscopical examinations, and, being an animal disease, the ease with which the same species naturally disposed to the disease could be had for inoculation and other experimentation, the etiology of pulmonary glanders still seems to be a debatable question, especially in one direction. As so often said, there can be but two possible ways in which a pathogenetic irritant can gain access to the lungs, except by experimental or traumatic introduction through the thoracic wall, viz., by aspiration of the inficiens, that is, by the respiratory passages, and metastasis, that is, by the circulation. These methods have been spoken of as direct or primary, and indirect or secondary invasion. While metastasis, or indirect invasion of the lungs, from a primary centre of disease in the nasal cavities or cutis is generally admitted in glanders, some very acute observers have been bold enough to doubt primary invasion by way of the respiratory passages, or the aspiration of the bacilli in the inspired air. This side of the question is more ably represented by

Dieckerhoff than any one else. He says: "That primary infection in the skin and in the mucosa of the nasal passages can occur in glanders is beyond all doubt, but the especial experiments here reported demonstrate the correctness of the opinion that the mucosa of the nasal passages as well as the cutis can also be infected by means of the blood circulation. The pathogenesis of the lesions of glanders in the lungs is brought into correspondence with many clinical observations through these experiments, viz., that the nodules, nodes, and other neoplastic products in the lungs can be produced through the transportation of the contagium by means of the circulation." "There are no anatomical conditions connected with the genesis of pulmonary glanders which justify the deduction that it is dependent on the primary introduction of the contagium into the alveoli. None of the experiments made since the time of Viborg have shown that the invasion of the lungs in glanders was directly produced through aspiration of the contagium." "From this condition of things the conception of primary pulmonary glanders is only an hypothesis. In my opinion no sufficient evidence has been brought forward in favor of any other origin for pulmonary glanders, no matter how varied the lesions, than metastasis."

In the same connection Dieckerhoff further says: "My not inconsiderable experience teaches me that primary affection of the nasal mucosa or cutis can take a most mild and superficial course and heal in a short time, without leaving any disturbance in the tissue indicative of previous lesions. Before such lesions have healed the contagium has been absorbed and conveyed to the lungs by means of the circulation (metastasis) and led to the development of various neoplasmata. In this way is developed a portion of those cases to which the name latent or occult glanders has been given. In the course of time infectious material may again find its way from the pathological centres in the lungs to the skin or nose by means of the circulation, and again give rise to the development of fresh disturbances in those tissues. For such consecutive or metastatic infection of the nose and skin the locality of antecedent infection is to be sought in the lungs. Nevertheless, the lesions in the lungs do not, therefore, acquire the character or importance of primary infection in relation to the total history of the disease in the case in question."

With many of the statements of Dieckerhoff I am entirely in accord, and in none more so than in relation to the mild superficial self-healing lesions in the nasal mucosa and cutis, a point particularly discussed in previous pages, and metastatic extension to the lungs and other organs, with secondary metastasis from the lungs to the nose and cutis again in the most unsuspected manner. Never-

theless, the evidence in favor, much of it derived from personal experience, of primary aspiration invasion of the lungs is so strong, and the circumstantial evidence is so important that one cannot ignore it so easily, notwithstanding serious objections already discussed, to which it may be well to allude again, and a strong inclination against too much stress in favor of aspiration invasion as the cause of primary glanders in the lungs. One of the greatest difficulties in the way of primary aspiration invasion in the lungs in glanders lies in the antagonism between laboratory experience in relation to the loss of virulence by bacillus malleus, especially on desiccation, and the necessity of desiccated material for aspiration infection. As said in earlier pages, if the glanders bacilli lose their virulence as reported, then they must become attached to hay or other stable dust and be aspired in that condition, or infection in that way is impossible, and Dieckerhoff's position is correct.

On the other hand, that the bacillus of glanders does not lose its virulence so quickly in stables must be true, or some other explanation must be found for many cases of infection, though it is well known that the "say so" of owners, grooms, etc., as to the presence of glanders in a stable, or as to the whereabouts of horses which may have become infected outside of it, is not always trustworthy. Still there is much reason for believing that there are conditions in which nasal discharge or other material has kept its virulence in stables, when the diseased animal has been removed. On the other hand, it is always possible that a second outbreak of glanders in such a stable may be due to later infection outside the stable, or to the almost entirely unappreciated and often unobserved mild infection of an animal or animals from the first cases, local healing with metastasis to the lungs and other organs, and secondary metastasis and an acute eruption months after the disposal of the first case in the stable.

So much for theory. Now for facts!

What explanation is to be offered in case of the two hundred and sixteen autopsies from the records of the Berlin school in which lesions of glanders were wanting in the nasal cavity in thirty-three, and the pulmonary lesions antedated those in the nose in more than half, while lesions failed in the lung in but ten? Although the history of any science is more largely a record of erroneous observation and misconception than success, except as a whole, still it is pretty difficult to believe that one of the most acute observers in the field of pathology should not see a nasal lesion in thirty-three cases out of two hundred and sixteen, if the lungs were generally invaded by metastasis from that region. The main difficulty lies in the ease with which slight, superficial, and healed primary lesions in the nose and

cutis may of necessity escape attention. It is pretty difficult to believe that so many good observers have let the "footprints" of primary glanders escape them so frequently as they must have if Dieckerhoff be correct. However slight and superficial they may have been, they must have left an impression.

On the other hand, it seems as if Dieckerhoff makes a fatal concession to the "hypothesis" of primary pulmonary glanders, and completely cuts his bridges behind him when he says: "The acute bronchopneumonic conditions stand only in loose connection with the contagium of glanders. Their origin is intimately connected with injurious etiological material which penetrates into the lungs with the atmospheric air. The ulcerated centres of disintegration—the caverns of acute glanders—find their genesis in part in metastatic embolism and in part in atmospheric influences." If bronchopneumonic centres and ulcerated cavernous conditions can and do find their origin in aspired materials, what reasons can be brought forward that primary pulmonary glanders may not be caused by bacillus malleus in the same way, if the germs can get into the air in a sufficiently dried and virulent form to be taken up and aspired?

That the primary lesions in the nasal mucosa are generally caused by bacilli in the aspired "atmospheric air" is admitted by Dieckerhoff, and it seems impossible for him to reconcile his statements against primary lung infection with the following: "The contagium of glanders gains access to the susceptible organs either from outside or through the lymphatics and blood circulation. In general the contagium is introduced from the outside to the primary centres of disease in which it multiplies. As a rule the superior parts of the nasal cavities are the 'atrium' for infection; the skin less often."

As direct traumatic inoculation of "the superior parts of the nasal cavities" is absolutely out of consideration, the bacilli can get there only through the inspired "atmospherische Luft," and must be in it. If in it, how can they all be so good as to light at this one "atrium" and not be carried "to the end of the route," that is, the termination of the bronchioles into the alveoli? It seems absolutely impossible that such an extensive diffusion of microorganisms by means of metastasis from a primary centre in the nose or cutis could take place as to answer for all neoplasms in the lungs, and "remain in the nutritive capillaries from whence proceeds the development of neoplastic products," as Dieckerhoff claims. With one more quotation we will leave Dieckerhoff and consider further evidence on the other side. If chronic glanders has a "feverless course," so long as the processes in the respiratory organs are not bound with diffuse bronchitis, to

what does the diffuse bronchitis owe its origin and its fever-producing character if not to aspired germs? This being so, why may not pulmonary glanders have the same source at times and in part?

The statements of so experienced and proven a knight in the arena of pathological investigation as Bollinger cannot be ignored when he says: "Apart from my own researches, which show most clearly that where glanders is inoculated the discharge from the nose and other nasal symptoms generally make their appearance as the final phenomena, . . . there may be found in the history of glanders in the human subject numerous instances in which the nasal lesions were developed only after the chronic affection had already existed for a considerable period," and quotes Hauff as saying that "out of seventy cases in man there were but thirty in which affections of the nose were found." It scarcely seems as if all these observations could be erroneous, and that in none of them were there lesions in the lungs of primary origin. On the other hand, primary lesions in the nose in man and aspiration invasion should both be the rarest forms of invasion. The assertion of Rabe and others that "the ulcerations in the superior part of the respiratory apparatus form an undoubted source of infection for the lungs," except by way of metastasis, is not worthy of serious consideration, being contrary to the anatomical and physical conditions in the parts. Insufflation metastasis is not probable in equines.

The lesions in the lungs which may be attributed to the glanders bacilli are the generally ignored neoplastic induration of the periarteriolic and bronchiolic tissue, in which nodules and nodes may sometimes develop from embolism in vessels within the diffusely complicated tissue and the nodules (tubercles), nodes, and irregularly contoured growths scattered through the lungs. The difference between acute and chronic glanders in the lungs is manifested first by the greater tendency to the development of nodules and small nodes, the great amount of hemorrhage in the centres, and the great tendency to ulcerative destruction instead of incomplete caseation, calcification, or organization. The large growths are peculiar to chronic glanders, and vary much in consistence, according to the general constitution of the animal and the vigor of its circulatory system. That all the circumscribed neoplasmata which may be rightly attributed to the glanders bacilli are of metastatic embolic origin, as asserted by Dieckerhoff; and especially that all the embolism of this character occurs "in the nutritive capillaries" or bronchiarterial system is not in accord with the anatomico-physiological condition. Such an hypothesis demands that all the emboli or loose microorganisms which may have started from a primary centre in the nasal mucosa, the cutis, or elsewhere, shall have passed both sides of the pulmonary

circulation, gained access to the left ventricle, and pass via the aorta into the bronchial arteries. This hypothesis is on a par with the assumption that glanders bacilli in the aspired air are caught by, or stop with, the mucosa of the superior parts of the nasal cavities, and that none pass with the air through the bronchial tubes into the alveoli. Were this the course of metastatic embolism in the lungs, the embolic infarctions would not have their characteristic V shape, nor would the lesions have much of their present character. But, what is of more contradictory importance, if the emboli or germs passed through the physiological pulmonary circulatory system, and it did not act as a dam or sieve to the degree it does, and did pass into the aorta, as claimed in this hypothesis, how can the other organs so prone to embolism in the arterial system, the brain, the kidneys, and the spleen, almost completely escape, and bacillary lesions in other parts of the arterial system, liver, muscles, etc., escape to the degree they do? How is it the coronary arteries of the heart generally escape invasion, and the bronchial are so particularly honored? There is no foundation whatever for such an hypothesis. Embolic infarction occurs in the so-called "end arterial" districts. Bacterial coagulation can occur in any capillary region under favorable conditions, but the conditions in the territory shut off would not bear any morphological resemblance to embolic infarctions on account of the influences of collateral circulation. In so far as the lesions in the lungs find their origin in metastatic embolism, in so far must the disturbance begin with the terminations of an end artery and extend from it, embracing the territory included in the arteriovenous capillary system thus shut out of circulation. The character of the resulting lesion will be determined by the virulence of the glanders bacilli and the freedom of the embolus from adventitious germs. If bacterial embolism took place in the nutritive capillary system to the degree claimed, there would be no chronic glanders. There would be *gangrena pulmonum universalis acutissima.*

In metastatic embolism in the lungs the bacteria in the embolus exert a double influence; by obstructing the circulation they lay the foundation for the infarction of the complicated territory, and through their chemical products they exert an influence on the terminal walls of the vein and the adjacent tissues, the influence varying with the virulence of the germs, the purity of their species representation, and the extent of the arteriovenous capillary anastomosis. Following on the reflux congestion comes a migration of cells, which in acute glanders give character to the lesion, as exemplified by its transient nature. Naturally, the presence of pus-generating microorganisms materially augments this condition; the necrotic condition extends

towards the peripheries of the infarcted portion of the lung, where begins cell proliferation from the connective stroma, which acts as a wall of defense against the farther extension of the necrosis and forms the so-called capsule. In this way the abscesses or cavities are formed in glanders. It sometimes happens that the gangrenous processes, as in the Schneiderian membrane, are so severe that they erode the venous stems in such sections, causing hemorrhages; in the lungs such erosions often extend to the bronchi, and then the hemorrhagic bacteria-laden material passes upwards and outwards through the respiratory passages, often infecting the mucosa of the bronchi and trachea. At other times more or less complete thrombosis of the veins in the complicated territory occurs. When the thrombi are malignant, germ-infested, secondary metastatic embolism may occur in other parts. If the embolism has been benign and is composed of glanders bacilli in a non-virulent or very mild condition, the resulting neoplasms, if tubercles, may undergo caseation and calcification, or even become fibroid tubercles; in the larger nodes there may be a caseated or calcified centre enclosed in a dense mass of organized tissue. When the embolism is benign and the process slow, the neoplastic tissue develops slowly and becomes densely organized, embracing the entire infarction; eventually this territory shrinks. A number of such territories in apposition may give rise to extensive, irregularly contoured masses of fibroid tissue—one form of indurated growths peculiar to glanders. In mixed bacillary embolism extensive cavities may be formed in similar localities, though not equal to those in tuberculous phthisis.

Notwithstanding the authority here presented, there is no doubt of invasion via the respiratory passages in glanders, frequently causing obstruction at the termination of the bronchioles, atelectasis and pneumonia in the complicated territory, neoplastic developments extending from the walls of the obstructed bronchiole as well as encroaching upon the peripheries of the bronchiolic territory; the same results with the same outcome may occur in this way as in metastatic embolism from the blood-vessels. Atelectasis, especially in old horses, may be present, due to chronic catarrh aggravated by the glanders complication. A thickening of the walls of the bronchioles along the catarrhal territory is common in old horses, as is also a tubercular development around their terminal end—bronchitis nodosa. Complication of the pleura and induration of the septa, extending from it into the lungs and the vascular and bronchial walls in the vicinity, is very common in chronic glanders. A very frequent disturbance in old, anæmic, weak-hearted horses in chronic glanders is extensive intravital thrombosis of many sections of the pulmonary

vessels, and intravital thrombosis in the heart, extending just prior to death into the large vessels proceeding from it.

Glanders in the Cutis and Subcutis—Farcy.

This localization of glanders in the horse is somewhat rare, although, as previously indicated, if slight, superficial, and rapidly self-healing lesions can occur in the superior parts of the nasal passages from aspiration bacilli, how much greater are the opportunities for invasion and similar lesion through abrasion of the epidermis or wounds of the cutis? Metastatic or secondary invasion of the cutis and subcutis by means of the circulation is claimed to occur much more frequently. The rarity of cutaneous glanders indicates that metastasis cannot occur very frequently. Cutaneous glanders is especially an accompaniment of acute or subacute glanders, and except in its elephantiac form is seldom seen in chronic glanders. The lesions bear much resemblance to those seen in the Schneiderian membrane. They may be either superficial, attacking the cutis principally, or profound when they include the subcutis in their embrace. They first appear as small nodes or nodules, or a nest of nodules, which soon soften and then break down and out on the surface of the skin; the edges of the "bud" are swollen, ragged, ulcerated, enclosing a crater-like base in which may be tubercles, the cavity being filled with a grayish-yellow, often hemorrhagic material of viscid character. The lymphatics from such a complicated portion of the skin are enlarged, indurated, and prominent in the cutis—farcy pipes—their appropriate gland or glands being also swollen, and in acute glanders the seat of manifold tubercle development and abscess formation or of tubercles of a more enduring character and induration. These superficially situated "farcy buds" frequently heal of themselves, leaving no traces behind them. It is a question if all of these self-healing cases of glanders in the cutis proper are not the result of direct invasion.

Glanders beginning in the subcutis is generally quite another affair, and of metastatic-embolic origin, or secondary invasion. The lesions are far more intense, the buds larger and more frequent, the necrotic disturbances far more profound; they have little or no tendency to heal. The surrounding cutis is more or less extensively œdematous, its blood-vessels are engorged, and its lymphatics are more seriously complicated, nodules appearing along their course. Neoplastic formation, both circumscribed and diffuse, may develop in the complicated territory; the tumefactions are sometimes very acutely developed and rupture unaided; the secretion from the cutaneous lesions in glanders is thinnish, viscid, discolored. The adjoining

tissue is swollen and œdematous. Gangrenous destruction of the skin is no uncommon occurrence in acute glanders causing severe ulceration.

Lymphatics and Lymph Glands.

As indicated in the previous section the marked complication of these organs in glanders is limited to the diseased territory which they drain. This has no reference to a general induration which the stroma of the lymph glands generally undergoes in chronic glanders. Persistent nodules are no uncommon occurrence in the glands when the disease is chronic, while tuberculous nests, necrobiosis, and abscess formation are common occurrences in territorial glands in acute cases. The induration in chronic malleus, or in glands previously infected from a local centre of invasion, frequently extends to the adjacent tissue, uniting it and the gland. Such glands have a hard, nodulated surface.

Spleen, Liver, Kidneys, Testicles, Bones.

In glanders, while the stroma of the three first-named organs is invariably diffusely indurated in the chronic form, other and more marked invasion occurs in the percentage in which the organs have been named. The rarity of metastatic bacillary infection passing the lungs is shown in the freedom of these organs, especially the spleen and kidneys, from embolic infarction and the customary lesions following the same in other organs. In chronic glanders the spleen is small, dense, indurated, anæmic, the capsule is thickened and of a whitish-gray color; occasional fibroid neoplasms are in its substance and often to be seen through the capsule or extending beyond its surface. In metastatic embolism, in acute or subacute glanders, the lesions have the usual character of a recent infarction; the pulp is densely swollen and dark red, extending beyond the surface like half a pea, cherry, or English walnut; in the centre of this mass is a grayish or yellowish centre made up of round cells; the infarcted portion pales out in many cases and is surrounded by reddened, engorged tissue. Calcification of the caseous centres of the neoplasm is no rare occurrence. Nothing more need be said of the other organs, the lesions being similar, but generally less in number and size.

Symptomatology.

The clinical symptoms of glanders can be briefly treated. The visible lesions, having been described, need not be further alluded to, save to say that as such the only symptomatic lesions are the ulcerations of acute or subacute glanders in the mucosa of the nose, or the ci-

catrices following their healing, and the nasal discharge connected with them, which is most frequently the one pathognomonic symptom in the suspicious sense. The cutaneous lesions have been described, and the condition of the lymphatics and glands taking the drainage from a diseased territory has been sufficiently alluded to. The evil effects of the previously considered teaching of Lafosse, that "true glanders is the discharge which comes alone from the nose," confronts the hygienist on every side in his intercourse with horsemen, scarce one of whom "knows glanders when he sees it," and all of whom will deny its existence unless the famed nasal discharge is present. Brochures have been written and learned pundits have gone mad as to whether both nasal cavities could be diseased at one and the same time, or the left nostril was more frequently the seat of a discharge than the right. Statistics show both cavities to be diseased in about half the cases, and each side about equally in isolated invasion.

The quantity of the nasal discharge varies with the virulence of the attack and the severity of the catarrhal disturbance of the unulcerated portion of the Schneiderian membrane. In chronic glanders the secretion is often so little as not to excite suspicion, while again the discharge may be quite profuse and viscid. Ofttimes the discharge has a yellowish or greenish hue, from the admixture of the blood-coloring stuff from disorganized red blood cells. The absence of fever in the presence of other suspicious symptoms in chronic glanders is of no importance, as that form may run for months and sometimes years without noticeable fever. Cough, difficulty of respiration, etc., have not the value once attributed to them.

Immunity.

Under conditions favorable to invasion, experimental inoculation with pure cultures of the bacillus being the most so, the majority of the domestic and probably the wild mammalia have what is termed a disposition to invasion by bacillus mallei. Cattle and swine are supposed to possess actual immunity. Whether or not they possess it to large quantities of virulent bacilli forcefully injected is not so evident. This question of natural and individual immunity is of such scientific interest and may be made of such practical importance that it is well briefly to touch upon the ground it is founded on in relation to glanders.

Notwithstanding the positiveness with which individual immunity to natural infection is often asserted, it is questionable if it exists in the members of any zoological species possessing a natural disposition to a given disease. It must not be forgotten that there is a wide

road and a vast difference between the conditions of natural extension and exposure to those of artificial inoculation, not only as to directness of contact with infectious material while in a virulent condition, but also as to the amount gaining access to the exposed organism. In artificial inoculation we are able to control the quantity of virus used, the place of inoculation, and the virulence of the germs in other susceptible animals, the results of which we are well acquainted with in the case of the guinea-pig in glanders. Under such conditions the result should be universal infection.

No such uniformity of infection can be expected under natural exposure. Of one hundred and thirty-eight healthy horses exposed in the same stable with glandered ones, cleaned with the same utensils and worked in the same harnesses, but twenty-nine became diseased. Lydtin gives the ratio of natural infection as from forty to fifty per cent. of the exposed. The inoculation experiments with nasal discharge or scrapings from farcy buds or abscess pus of prebacterial medicine, made in horses without mallein tests and with no control in guinea-pigs of the material injected, have no comparative value whatever, as in many cases there may have been no bacilli in the material used or so few as not to cause infection. Negative results in such cases give no evidence of value for individual immunity. If such a thing exists it can only be determined by the inoculation of not less than one hundred young, healthy, mallein-tested horses at the same time, with the same quantity of the same material introduced in the same place in each animal, controls on guinea-pigs, one for each horse, being also made.

The literature of glanders frequently mentions cases, which daily experience is corroborating, of a well horse being worked by the side of a visibly diseased one, with nasal discharge or farcy buds or both, sometimes for months (sixteen months is the longest known to the writer), the animal remaining well and for years under the alert observation of a competent veterinarian, who often finds opportunity to make an autopsy, and no glanders is found. Dieckerhoff in his "Pathologie" gives two such cases which he observed for five years respectively, and made an autopsy on one. Other horses in the same stable became diseased, supposedly from the diseased one.

Such cases only show the difficulties in the way of the extension of glanders under certain natural conditions. They contradict the traditional assumption of a volatile virus, and speak for the necessity of inoculation by accidental abrasion or "dust" infection. The most rapid and extensive spread of glanders I have ever seen has been in range horses corralled for the winter, that were fighting, kicking, and biting all the time.

As severe constitutional disturbances, the intervention of other diseases, or a surgical operation may serve to transform chronic into acute glanders, so conditions weakening the constitution, convalescence from other acute diseases, or polyuria, may give a predisposition to infection in individuals which in no way should be classed as a natural disposition. There is no evidence of natural immunity in horses against glanders. There is some little evidence that cases of glanders do occur in which healing by natural limitation takes place. We know of many cases that at the time present completely healed nasal complications, but pulmonary lesions remain for years, and the animals are the most dangerous of all because not suspected. Dieckerhoff mentions such a case that he knew of for seven years; the horse worked all the time and would certainly have lived longer had it not been killed for other causes.

The above remarks will serve as a fitting introduction to the question of

GLANDERS IN MAN.

Etiology.

Taking a superficial view of the case and following the general tenor of the literature on the subject, it might be said that man is not especially disposed to glanders, in fact, that he possessed a high degree of immunity. "The affinity of man for glanders is moderate, not to say slight. When the manifold opportunities for infection are considered, especially during the handling, examination, and necroscopical dissection of diseased horses, and the number of persons thereby infected is compared with the vast number that escapes infection, the correctness of this position is self-evident."

The above statement is open to most serious question. In point of fact it does not touch the question of immunity at all. What it does show is that the percentage of infection in man is extremely small, even among those most frequently exposed to infection. It warns against "sensational scares." So far as immunity goes there is no reason to doubt that man has as strong a disposition and offers as favorable a soil to the bacillus of glanders as any other susceptible mammalia under the same conditions. Considering infection alone, and not its result, it is doubtful if, inoculated in the same manner and in proportionally the same quantity and virulence, the germs of glanders would not find as favorable a stamping-ground in man as in solipeds. There is a difference between immunity which makes invasion or infection impossible, and resistibility which lessens fatality. Natural immunity consists in chemical conditions, making the inva-

sion of the parasite actually impossible, or making it impossible to secrete or produce a pathogenic material. Resistibility may be said to be a natural non-susceptibility to its action with varied limits as to fatality. In this sense man *may* be more resistible to glanders than horses. More cases seemingly recover. This statement needs to be taken *cum grano salis*. There may be cases of recovery in horses, but as all are killed as fast as they come within the clutches of the law, we know nothing about it. It is a tradition that such used to be the case.

The above-quoted remarks speak strongly for traumatic infection as the chief factor in the infection of healthy individuals. Herein to a large extent lies the secret of much individual immunity. Can self-healing occur in case of slight infection with very much mitigated germs, without general invasion? All that has been said in regard to the frequency of infection in horses may be equally true of man. Sometimes glanders extends in a stable not only rapidly but by most singular skips and jumps, singular only because we know not what has occurred, the most distant horse in a row becoming infected first, while those in the two adjacent stalls to a diseased one escape, all receiving the same treatment. At other times, a diseased horse may be in a stable months with no extension of the disease. "Individual predisposition," we are told. The facts are against it. Suppose we should apply the test of inoculating all with a large quantity of a virulent culture, what would become of this mysterious "individual predisposition"?

Glanders is a vocation disease; that is, human beings whose business it is to use or attend to horses are the only ones liable to become diseased. Women are more exempt than men, and children than women, because less frequently in contact with diseased horses, though women and children have been infected from sleeping in the same bed with a diseased husband or father, and healthy horses have been inoculated from diseased men; so have many guinea-pigs of late years, all of which goes to show that the bacilli do not lose in virulence in man, at least for a long time. The writer inoculated a male guinea-pig from a case of six months' standing in a man, in which no diagnosis had been made. The effects in the guinea-pig showed no variation in time of appearance of visible lesions or fatality. Hence the disposition, the nutritive conditions offered, must be pretty nearly equal in man and in the horse. The conditions of invasion are far more unfavorable. The text-books all give the idea support that exposure and immunity are closely related terms in such a disease as glanders. They have absolutely no connection. Take the late outbreak of Asiatic cholera in Hamburg with some twenty thousand cases

and ten thousand deaths (I write from memory, the lesson is not lessened in value by a slight error in figures), with no deaths among the physicians in attendance, the nurses, or the official hygienic corps. Was this due to individual immunity? Could exposure have been greater? Most certainly it could. The "immune class" were rigidly circumspect in their deportment. The ignorant class were not, nor would their surroundings permit of it. Nevertheless one reads of "the marked immunity of the medical profession and attendants" in that outbreak, as if it was something individual. The vocation susceptibility in glanders is of immense prophylactic importance; otherwise it has no value. Immunity in human beings in glanders depends entirely on the nature of the exposure, and the condition of the bacilli exposed to in regard to virulence. The conditions are exactly the same as those illustrated by the Hamburg cholera outbreak. A person may be most intensely exposed as an individual and yet not physiologically or pathogenetically exposed in any sense of the word.

In the preparation of this and the following article every endeavor was made to obtain some exact information as to the extent of glanders and anthrax in man in different sections of the country, but with no satisfactory results, except from the State Board of Health of Massachusetts and the Board of Health of New York City. These two reports are so instructive that no argument is necessary to support the lesson they teach of the necessity of the most reliable and detailed vitality statistics, in an etiological sense, for the purposes of legislation. In Massachusetts, from 1859 to 1875, thirteen deaths from glanders are reported. But it is to the statistics from 1888 to 1898 that especial reference is made. During this period there were eight deaths recorded from glanders, all hostlers, and sixteen deaths from anthrax among handlers of hides and curled hair.

The report of the New York City Board of Health is still more interesting.

	Glanders.	Occupation.	Anthrax.	Occupation.
1888.....	1		1	—Unknown.
1889.....	0		4	One laborer, one dry-goods clerk, one boiler-maker, one carman—all from handling dry hides.
1890.....	0		3	One plumber's assistant, one laborer, one musician—contracted disease in handling a hair mattress.
1891.....	0		0	
1892.....	0		3	—One unknown, one tailor, one mason.
1893.....	1	—Hostler.	2	—One unknown, one driver.
1894.....	0		1	—Teacher.
1895.....	0		1	—Laborer.
1896.....	0		0	
1897.....	0		1	—Unknown.

If that is not an interesting mess to unravel, where can one be found? It is easy enough to comprehend how laborers, drivers of drays, and persons handling hides should acquire anthrax; but the dry-goods clerk, the boiler-maker, the plumber's assistant, the tailor, mason, musician, and teacher, increase the number of vocations to such a degree and magnify the possibilities of infection in anthrax so greatly as materially to "mitigate" the immunity of mankind to a disease once supposed to be generally limited to curled-hair workers, hide handlers, veterinarians, and knackers. With the proportion in Massachusetts of sixteen to eight in favor of anthrax and sixteen to two in New York City in the same period of ten years, some might think it justifiable to speak of the greater immunity of man to glanders than to anthrax. Such does not exist, conditions being equal. On the other hand, should these statistics faithfully represent the vital ratio between anthrax and glanders for the country, they indicate the necessity of a much calmer and less sensational aspect towards glanders and much greater circumspection in relation to anthrax by health officials and legislators.

Manner of Invasion.

While man may be said to be an ignorant active or careless active factor to his own injury and that of his equine property, the horse is an intellectually passive factor in the etiology of glanders. "Volatile poison" still plays the great rôle of the sporadic or spontaneous etiological factor. It should be looked upon as identical with aspiration invasion or "death from causes unknown." No other version will cover such volatile ignorance.

The evidence at hand, though entirely wanting in detail exactness in regard to invasion in man, speaks for cutaneous infection in the majority of cases. The evidence of aspiration invasion is simply wanting in all positive characteristics. That bacillus malleus can invade a host via the intestinal tract and produce glanders, notwithstanding the experiments of Decroix in eating the flesh of glandered horses, cooked and uncooked, which was not so very dangerous after all, and that human beings, horses, or other animals can be infected by drinking water from a pail or vessel out of which a glandered horse had previously drank, has been experimentally proven by M. Eduard Nocard, who, after testing twelve horses with mallein and finding them free from glanders, caused them to drink (November 30th, 1896) a certain quantity of water to which a given amount of a known virulent culture of glanders bacilli had been added. After showing visible ni-

dications of infection in about eight days they were all again tested on December 15th, 1896, and all reacted. On January 21st, three were so much diseased as to have to be killed. This being so, is it not evident that in chronic glanders, when a disease centre breaks into a bronchial tube and the material is raised to the pharynx and swallowed, as most of it must be, the manure must contain bacilli and may be a possible means for air pollution and aspiration infection? The facts do not show that there is any more danger of invasion through the uninjured cutis than in tuberculosis, syphilis, anthrax, and many other diseases constantly subjected to necroscopical examination.

In the *Veterinary Journal*, of London, Vol. IX., there is a very interesting and instructive account of a case illustrating the danger possible in the nasal discharge of a diseased horse, though practical experience warns against exaggerating the possibility. Over a stable was a tenement, the steps to which came down by the stable door. A woman living in the tenement had a nursing babe. On taking it down the stairs one day, as she arrived at the bottom, a horse being led out at the moment snorted and some of the material fell on the child's face. The child acquired glanders. A sister who nursed the child acquired the disease from the nasal discharge of the child coming in contact with her nipples. Both died of glanders.

The only source of danger to man is in and from the glandered horse, though man can become infected from a diseased man or other animal than the horse, or from or with the discharges from a diseased horse polluting mangers, nails, woodwork, grooming tools, blankets, etc. So many are the ways of infection by means of slight wounds of the cutis, so uncertain is the evidence of infection by atmospheric pollution in man, so contradictory are the results of laboratory observation and practical experience regarding the vitality and virulence of bacillus malleus that the utmost caution is necessary in considering all cases of glanders not certainly due to cutaneous infection. It has been shown sufficiently that atmospheric infection is possible. Successful prevention lies in exact knowledge of the value of all etiological factors.

Symptomatology.

The same practical differentiation of glanders has been made by clinicians in man as in the horse, *acute*, *subacute*, *chronic*. In the acute cases the initiatory stage is from three to five days, the disease running its course in from eight days to two weeks. In subacute cases the prodromal period terminates in from ten days to two weeks,

the duration being from three to six weeks. Chronic glanders has no definite initiative stage and includes all cases extending over six weeks.

Acute and Subacute Glanders.

The disease is often ushered in by a general feeling of weakness, headache, and chills, so that with no history and no suspicious lesions the physician might be misled, and assume a malarial complication. On the other hand, ill-definable pains in the limbs, both muscular and articular, might lead to the suspicion of rheumatism. The fact that fever is often absent might still more mystify the case. The appearance of definite disturbances of a limited or diffuse nature in the skin or subcutis, especially around the joints, may soon set the diagnosis in the right direction. If a wound or an abraded surface has given the atrium to the inficiens, pains in such a locality, followed by hyperæmia and swelling of the lymphatics leading from it, may be expected. At this stage of the game a rise of temperature, sometimes transient, again permanent or intermittent, may be expected. The circumscribed lesions soften, break down, ulcerate, and, if not present at first, appear in the tumefied, œdematous tissues; the erupted nodules much resemble those in the horse in having rough, granular edges and base, covered with a dirty purulent material, the general appearance being most decidedly unpleasant, with little or no tendency to healing. When the wound is on the hand, there is often a hyperæmic, œdematous swelling of the arm, the lymphatics and axillary lymph glands being decidedly prominent, pustules and ulcers developing. Such severe complications in an acute toxic disease must of necessity be accompanied by gastric and intestinal disturbances; the appetite diminishes or is entirely wanting, constipation is often present, the general weakness augments, while the muscular and articular pains increase and the fever becomes more poignant and constant. As the disease progresses cutaneous lesions in the form of sharply defined red spots which develop into pustules, reminding one of variola, appear; sometimes they take the form of vesicles filled with a serous or serosanguineous fluid. When these lesions rupture, the result is most offensive to both sight and smell. Frequently circumscribed tumefactions and abscesses make their appearance, which are excessively painful, being hard at first but gradually softening; when opened, or opening of themselves, they present an ulcerated, ragged interior surface covered with a grayish-white coating. These abscesses often extend so profoundly as to complicate tendons, bones, and joints. While these lesions frequently develop almost simultaneously with the first indications of disease, in subacute cases

they tarry in their development and appear in the course of two, three, or four weeks; the same is the case in regard to the nasal discharge, which, as previously mentioned, does not appear so frequently in man as in horses. The nasal discharge when it first appears is a watery, viscid material without much color. The nose is swollen, particularly at the base and over the bridge, the tissues and those of the environment being hyperæmic, painful, and supersensitive, much as in erysipelas. The discharge becomes more viscid, purulent, often hemorrhagic, and generally offensive. One or both nasal passages may be implicated. Tubercular neoplasms around the alæ may be often seen, followed by the development of pustules and ulcerations in the mucosa. In very virulent cases the disease extends to the cartilaginous tissues, perforating the septum and vomer. Implication of the mucosa of the oral cavity and other parts of the respiratory apparatus may appear at or about the same time, as shown by ulcers in the mouth, invasion of the larynx, swelling of the lymphatics and glands which may become severely inflamed; pus may form, and eventually an abscess may break externally. The intestinal disturbances may augment in intensity, diarrhœa following the constipation. In such cases the oral cavity becomes disgustingly dry, coated, blackish-red, much resembling that of a dog or man suffering from hydrophobia, except that the patient can satisfy his thirst, which is naturally excessive. Cerebral disturbances varying from severe headache or intense nervousness to delirium may appear in the course of the disease, according to the virulence of the attack and the accompanying lesions. As in the horse, albumin is frequently present in the urine. In subacute cases intense prostration appears in the third or fourth week, accompanied by marked emaciation owing to the augmenting fever; the cerebral disturbance increases, the heart becomes weaker, the circulation poor, the body cold, respiration weak, and death ends the scene, the nasal or cutaneous discharges having become indescribably foul.

Chronic Glanders.

The essential apparent difference between chronic glanders in man and horses is that while in the latter glanders has the reputation of being invariably fatal in any form, in man about fifty, or a very large per cent. eventually recover by natural limitation, the illness always continuing for months and often for years. This looks like evidence of lesser susceptibility and more unfavorable nutritive conditions for the toxicity of the bacilli than in horses, but where and what is the evidence? There can be no question that three factors may play the

essentially lethal rôle, singly or combined, in glanders: (1) the toxicity of the glanders bacilli; (2) the toxicity of adventitious germs; (3) the toxicity of destroyed tissues plus loss in organic action as the result of the first two. In chronic glanders it is very difficult to value these factors correctly, more especially in a comparison between man and horses. A marked pathological point of difference, which must find its cause in constitutional differences, is the greater tendency to superficial abscess development, the involvement of the tissues around the joints, and the greater amount of fever in man than in horses; and yet in the face of all this, we are led to assume that recovery is more frequent in man. There is room for work here and careful observation. It is a rare, almost an unheard-of thing to find a horse actually dying of chronic glanders at the present day. The veterinarian seldom sees one. The law takes care of them ere that time arrives.

That the difference between acute, subcute, and chronic glanders must be attributed to variations in the virulence of the bacilli in the first place, and not to individual idiosyncrasies of the host, is borne out by the fact that the transmitted disease generally assumes the same course in the majority of individuals infected from the same primary host, a condition long since noted in variola and confirmed by laboratory experience. Put in other words, it is a sort of law of infection that, given the same species of animals all equally healthy, and the same amount of toxic pathogenic germs inoculated, microorganisms of the same culture or virulence will produce approximately the same results in the infested hosts.

Chronic glanders begins with phenomena similar to those of subacute, of which in a milder form it is but a continuance. If the invasion of the bacilli has been by the respiratory tract, without occasioning primary lesions in the nasal passages, and the disease processes are developing in the lungs, aside from general malaise, nervousness, intermittent attacks of fever, sometimes none, and pains in various parts of the body, the physician may be absolutely without any reliable diagnostic data, unless he may fortunately have obtained a corroborative or suspicious history. If the *locus invasionis* is in the skin or nasal passages, the afore-mentioned local swellings, eruptions, discharges, lymphatic implications will appear, but in a much less malignant and often scarcely suspicious form, and may even entirely disappear. This being a frequently observed condition and being due to the virulence of the bacilli, does it not justify the assumption, so strongly contended for here, though not with the idea of lessening the importance of primary aspiration invasion in the lungs, that superficial cutis or nasal invasion may take place with secondary

invasion of the lungs? In such cases the bacilli must enter the blood via the lymphatic system without causing local disturbance enough to attract attention, or at least suspicion.

When local lesions occur as evidence of invasion in chronic glanders, they might be said to be subacute lesions in *statu quo ante.* They remain a long time in the same condition—nasty ulcerous chancres, with but a slight tendency to healthy granulation, though they may eventually heal by the formation of correspondingly extensive cicatrization. New abscesses may continually spring up in the vicinity of old and partially healed ones, nodules of various sizes (erupting into small ragged-edged ulcers) appearing between them, the lymphatics suffering in corresponding degree. Only those who have had personal experience can appreciate the difficulties of reducing the walls of these opened abscesses to healthy granulations. Their contents cannot well be called pus; we find rather a mixture of serosanguinolent material and round cells, mostly if not entirely migratory. At times, if no abrasion of the cutis has occurred, this material may be practically germ-free on microscopic examination, and if the abscesses are opened under proper precautions with the thermocautery, the stuff may appear germ-free in cultures, unless an excessive number of tubes is inoculated. On the contrary, the immediate intraabdominal inoculation of a male guinea-pig with the same material may bring the desired pathognomonic result in from two to three days. As of cutaneous so of nasal localizations, they may be entirely wanting in about fifty per cent. of the cases, and they do not apparently stand in any such proportion as a primary lesion as does cutaneous glanders. When present, the necrotic processes may be of the most destructive character, bearing resemblance to those of syphilis. The mucosa of the oral cavity also suffers in like degree with inflammatory and ulcerative conditions, having a retarded tendency to heal. The discharges are viscid, serous, seropurulent, seropurulent and sanguineous, varying much in quantity but not so much in offensiveness. The upper part of the respiratory tubes, the larynx and trachea, may be similarly involved, as shown by hoarseness, coughing, raising of a vile sputum, and sometimes their mucosa is so swollen as to make inspiration difficult. In connection herewith the patients may emaciate excessively from the pain, fever, and disturbance of the digestive functions. As in the horse so in man, chronic glanders may suddenly assume the acute form through metastasis, characterized by similar local conditions. Death may result in coma and general collapse. When chronic glanders terminates favorably the prognosis can be made quite early in the case, provided the diagnosis be correct. From the beginning the local lesions are characterized by their slow-

ness in development, and though innumerable swellings, nodes, and abscesses may come and go in the course of the disease, especially about the joints and cranium, still there will be an obstinate though protracted and disappointingly slow tendency to heal, which of itself is a suspicious diagnostic point. Naturally the discharges slowly decrease with the disappearance of the local disturbances. There may be cases of primary pulmonary glanders, mild in their course from the beginning and uncomplicated by metastatic local disturbance, which run their course without giving evidence of their nature, when their origin is not suspected by patient or physician. We know it is so in tuberculous phthisis. The autopsy table reveals that fact. Is it going too far to assume that it may also be so in glanders in man and probably in the horse also?

Pathological Anatomy.

That metastatic bacillary embolism plays as essential a rôle in human as in equine glanders is made evident by the general impression of pyæmic processes, "wedge-shaped abscesses" and infarctions, which the lesions impress on the necroscopical observer. For this very reason the tendency to abscess development in man is more marked, while that to circumscribed neoplastic indurations is less marked than in the horse. The fact that the lungs are less frequently implicated than in the horse speaks strongly for the predominance of local, superficial, exterior invasion in man over primary pulmonary invasion. Metastases from the lungs to the skin and other organs, spleen, brain (abscesses), are even more common than in the horse; such metastases may result from primary aspiration invasion, pulmonary lesions, or secondary invasion of the lungs by metastasis from local cutaneous or nasal lesions.

A description of the lesions of glanders is largely a repetition of the clinical history of the disease, so far as it bears on visible cutaneous or nasal lesions. As particularly noted, the cutaneous pustules frequently bear a resemblance to variolic conditions, while in others they are more vesicular and filled with a serosanguineous fluid; the abscesses have not the character generally considered pathognomonic of such lesions, but more nearly resemble a sort of dissolving process, the tissues around looking as if semi-dissolved where they form the walls of the cavity, which is filled with a thick, creamy, grayish red, viscid, serosanguineous material. These abscesses sometimes penetrate the aponeurosis of the muscles and implicate the muscle substance; at others they extend to the bones, particularly of the skull, causing necrosis, the irritation penetrating through the skull

and causing a pachymeningitis malleosa which may be purulent or tubercular in character. Softening of the substance of the bone occurs.

The lesions in the nose resemble those in the horse and need no special description. The same may be said of the sinuses, the pharynx, the larynx, and trachea. As previously said, the lungs are less often the seat of primary lesions than in the horse, but when present these are largely of the same character—tubercles, nodules, and more diffuse processes—even to considerable indurations of a pneumonic type. Abscess development is not uncommon. Peculiar complications, ante-mortem thrombosis in the veins, hemorrhagic, œdematous, and anæmic gelatinous infiltrations, so common in old horses diseased with glanders, are not seen so often in man, perhaps because the majority of cases are in young vigorous men, while for the same reasons (economic) they are largely among old and cheap horses, except when the disease gets into breeding or agricultural districts. The muscles are far more frequently implicated than in the horse, more particularly those of the arm and breast.

The localizations in the bones and the oral cavity have been mentioned. Ecchymotic lesions in the mucosa are common, the stomach not escaping; but they are seldom if ever seen in the horse. Parenchymatous changes from cloudy swelling to fatty degeneration are to be expected. The general lymphatics are less affected than in the horse, and in man there is no evidence of the diffuse involvement of the stroma that there is in chronic glanders in the horse; but as this is a personal observation in horses the estimate may be erroneous, that lesion in horses not being mentioned by the authorities. The tendency to incomplete development of tubercles and indurated neoplasms has been previously mentioned as peculiar to glanders in man.

Diagnosis.

Some twenty years ago Bollinger wrote: "The diagnosis of glanders is in many cases extremely difficult if not absolutely impossible. The last is especially true in cases in which the lungs are the chief seat of the trouble, or in which the disease processes are seated in parts withdrawn from observation." The same words were equally true of glanders in man, especially when the anamnesis is untrustworthy or entirely wanting. But time brings changes with it, and among them is the comparatively infallible diagnosis of glanders through the use of the material known as mallein, of which somewhat has been said in previous pages, and more can be learned by reference to Vol. XIII. of this work. Mallein can be purchased of most of the large whole-

sale drug houses. It is a pale, amber-colored liquid. Two and a half cubic centimetres of this fluid is injected under the skin of the patient in which glanders is suspected. The skin must be first washed and disinfected over an area the size of a silver dollar, and if hairy should be shaved. The temperature of the patient should be taken night and morning for the two days antecedent to the mallein injection. If the patient has glanders, there will be a marked and progressive rise of several degrees in the temperature, commencing a few hours after the injection. The place of injection swells, often excessively, and is painful. In case mallein is not at hand, resort may be had to the inoculation of a male guinea-pig—safer if two or three are used—with the nasal or cutaneous secretion of a suspected case, or the contents of an abscess, or if they are wanting, a swollen lymph gland may be removed. The injection should be in the abdominal cavity. Peculiar swelling and purulent implication of the testicles and their sheaths will appear in from two to five days. As all other cases of glanders are easily recognized by competent persons and the visible lesions have been sufficiently discussed, they need not be further considered. Unlike the veterinarian the physician lies under the difficulty due to the rarity of his cases. In case of suspicious cutaneous lesions or neoplastic products, abscesses full of a vile grayish-red generally not ichorous fluid, with lesions in the surrounding skin of an erysipelatous or phlegmonous appearance, the physician should have recourse at once to male guinea-pig injection.

Prevention.

The only cause of glanders in horse and man, so far as human knowledge extends, is and has been the obligatory host of bacillus malleus, the diseased horse. Could every glandered horse in the country be removed, which is practically possible by the combined use of all our means of diagnosis and disinfection properly carried out, an end could be made of glanders in horse and man forever, as has been done in the case of contagious pleuropneumonia in cattle, unless new cases were introduced from outside the country. Given the diseased horse, the dealer in cheap horses and those who work such in numbers are the chief and most dangerous factors in the extension of glanders. All horse dealers should be licensed and be held criminally responsible for the sale of any horse having visible symptoms liable to cause a suspicion of glanders, without having previously reported it to the authorities. Owners or grooms taking care of such "suspects," with nasal outflow or skin lesions, should be held equally liable with dealers for not reporting such to the authorities. More

attention should be given to public drinking-fountains, which should be flushed all the time with good outflow. Special officers should be employed to scrub them out every morning before 8 A.M. More attention should be given to the vitality-virulence of the bacilli under ordinary stable conditions by the study of the materials polluted by glandered horses at different periods after death or removal, giving time to pollute everything in its stall. The manure question requires attention as a part of the atmospheric infection problem which demands long and exact revision with the utmost experimental detail.

Treatment.

Treatment is out of the question except in man, and in case of exceptionally valuable horses that can be isolated so as not to endanger others. Whether or not mallein has permanent curative qualities, or whether a germicide that is reliable can be gotten from bacteria, is a question for the future. An antitoxin alone will not do the work in glanders as in tuberculosis.

ANTHRAX.

BY

FRANK S. BILLINGS,

GRAFTON, MASS.

ANTHRAX.

Definition.—Anthrax is an acute, exogenous, facultative, parasitic, infectious disease, which is never general in its extension, but invariably finds its locus of primary origin in telluric and caloric conditions of certain localities which supply the pathobiological necessities of its specific cause—bacillus anthracis; and which is extended from such primarily infested localities by animals infected thereon to other localities, either by means of their natural excretions or by materials derived from such animals when dead—wool, hair, hides; and occasionally by floods.

Etiology.

Anthrax, or, to speak more correctly, the collection of septic diseases characterized by a purplish-black, thick, semi-coagulable blood in the cadaver, enlarged spleen, hemorrhages, and a sharp, quick course, is probably not only the oldest, but the best known of all the diseases which have come to us on the current of tradition and history. The first rupture of the continuity of this collective conception of anthrax was given by Pollender in 1855, and independently by Branell in 1857, both of whom saw that the blood of certain animals diseased with anthrax (it happened to be a case of true anthrax they had before them) contained numerous rod-shaped bodies, which excited their curiosity, and later that of the investigating medical world. No one guessed at their true nature for a long time. They were looked upon as crystals, as fibrin formations, as curiosities of no etiological importance, and having no connection with the disease. Finally, a suspicion began to develop in men's minds that these microscopic, structureless, apparently innocent, rod-like bodies could not be so constantly present in a disease presenting common and universally recognized phenomena without having some important connection with it. This suspicion developed into a certainty and was proven to be thoroughly justified by Davaine in 1863, although it may be said that the pathogenic history of bacillus anthracis and the complete differentiation of anthrax, as a disease *sui generis*, from the group of anthracoid diseases, was not effected until the publication of the masterly work of Koch in 1876. Anthrax enjoys the place

of honor among all the pestiferous diseases, because, more than all others, the study of its microorganism has opened the way to the investigation of parasitic infectious diseases. The great size of bacillus anthracis, in comparison with the majority of pathogenic microorganisms, brought it within the range of the microscopes of the times; the ease with which it can be discovered, cultivated, and inoculated successfully in experimental animals still gives to anthrax and its bacillus the first place in the interest of students and investigators. Convenient as this microorganism is to work with, much as has been done with it, there remains much more to be done. The ex-host, or better, pre-host, life of bacillus anthracis still awaits investigation. Notwithstanding Hueppe found a bacillus morphologically and in cultivations identical with bacillus anthracis, the actual discovery of that germ in its native heath, in a pathogenic condition, awaits confirmation. Even the chemical products, the toxins, by means of which the bacillus produces disease, have not been isolated as definite and tangible things, with which direct and satisfactory experiments can be made. While we should and probably do know more about anthrax than any other germ disease of which the parasite is known, still, when we ask ourselves, What do we know? it must be admitted that we know very little indeed of those essentials of which it is necessary to know so much in order to understand anthrax and kindred diseases.

Bacillus Anthracis.

If one has a suspicion or knows that the case before him is anthrax, if there is not a local lesion, as is frequently the case in man, and desires to confirm his diagnosis, all that is necessary is to draw a few drops of blood either from the local lesion or a vein and examine it microscopically, or introduce it under the skin of a mouse, guinea-pig, or rabbit, and the animal will generally be very ill within twenty-four hours, and perish between that time and forty-eight hours or three days from the date of the inoculation. Sometimes when we examine the blood drawn from a vein of the patient we are not able to discover the bacilli after most careful search, as they are often very scarce in the blood until just before the death of the patient, but the sickness and death of the inoculated animal indicate their presence in the blood. On the contrary, when the blood is taken from a local lesion the bacilli are present in goodly number. If we turn now to our inoculated animal we shall find an abundance of bacilli in the blood, the pulp of the spleen, the liver, the lungs, the kidneys, and other parts, scarcely one part being free, as they are well distributed in the blood-vessels.

It is not necessary here to go into the details of the examination and cultivation of this best known and easiest cultivated of all pathogenic microorganisms. For that the reader is referred to the text-books on bacteriology. Suffice it to say, bacillus anthracis colors easily in aqueous solutions of all the aniline dyes, the best for a practising physician being the tubercle bacillus mixture of one per cent. fuchsin, ten per cent. commercial alcohol, and ninety per cent. of a five-per-cent. solution of carbolic acid. This one dye will cover all needs, so far as coloring bacilli are concerned. The anthrax bacillus will not stand fading out, but unlike the tubercle bacillus it has morphological characteristics as distinct as is the technical reaction of the tubercle bacillus, by which it is so surely recognized. These characteristics are the size of bacillus anthracis, its square chopped-off ends, and its immobility, which are not those of any other pathogenic bacillus known. The bacilli will grow in or on any of the media used for that purpose and at room temperature. While perfectly safe, like venomous snakes, they need to be handled with care, and one must use the utmost precaution not to prick or injure the skin, and should not make a necroscopical examination nor handle anthrax material with fresh abrasions of the epidermis on the hands. For the phenomena of cultivation the reader is referred to the text-books or the appropriate volume of this work.

Constitutional or Internal Causes.

These can be handled briefly as they consist only of that physiological chemism natural to a species which offers suitable soil for the biopathological necessities of bacillus anthracis. The susceptibility to anthrax is very widely spread among the domestic and wild herbivora, Algiers sheep, for reasons unknown, not possessing it. Of fowls, white rats, frogs, and such things, it is not necessary to speak. They simply form curiosities of experimental investigation. As a rule the carnivora are more or less immune to anthrax and the anthracoid diseases. This fact has been quite prettily illustrated by experiments. If dogs or rats are fed on a strictly carnivorous diet they are immune to any ordinary amounts of bacillus anthracis, no matter how virulent. If, on the other hand, we turn such animals into herbivora and feed them on an exclusive vegetable diet, they gradually acquire a varying degree of susceptibility to anthrax. Can anything more clearly demonstrate that disposition is nothing more nor less than the physiological chemismus of the organism infested?

External Causes.

What internal causes are to endogenetic diseases, external causes are to exogenetic. In other words, what the physiological chemismus of a favorable species is to an obligatory parasite, local conditions, the chemismus and physical conditions of the soil, temperature, and moisture are to the facultative parasites. How long it is going to be before modern scientific investigation awakens to this fact is a doubtful question. While in endogenetic diseases external causes chiefly play the part of mere transmitters of the inficiens from healthy to diseased individuals, or serve as vehicles for the temporary protection of the parasite, in exogenous diseases the infested locality has the same relation to the healthy as the diseased animal in endogenetic; that is, it is the locus of primary origin, the seat of continuous danger. The question of *contagion*, of transmission in the course of the disease, is an entirely different matter with which we have nothing to do at present.

To make it still more plain: In exogenous diseases the parasites are permanent inhabitants of suitable terrestrial localities, but "can," under certain conditions, inhabit the animal body; while in endogenous diseases the parasites are permanent inhabitants of animals, but may exist for a longer or shorter period outside of them. There is this vast difference between them: While exogenetic parasites retain the faculty of proliferating in the infested host, the obligatory parasites do not in ex-host conditions. It is these two conditions of the primary origin of infection which classical medicine endeavored to express in its axiom, that "while all contagious diseases are infectious, all infectious diseases are not contagious." Anthrax in either its collective or individuated sense stood for that class of infections which classical medicine differentiated as "not contagious." Nothing could more plainly show that our predecessors had primary origin and not extension-transmission in mind when they made such a definite differentiation. It will be remembered that we have been told that a "marked difference must be made between ectogenous (exogenous) infection, in which the bacteria can flourish outside of the body, and endogenous infection, in which they flourish only in the diseased body."

As stated in the preceding article on glanders, the point in discussion is the value of that word "can." Is it possible that any one can read the above and not be forced to the conclusion that the "can flourish outside of the body" or animal host means that that condition must be looked upon as the unusual, and not the regular,

form of life of such parasites? Assuming that to be the case, what "can" be the difference between exogenous and endogenous parasites? It being admitted that both do live in animals and both do cause disease, and that both do live in ex-host conditions, what can be the difference between them? Both forms can and do multiply and replenish their kind in the animal host; both forms can be transmitted, in some way, from diseased to healthy hosts, and thus the disease is, or may be, continued and extended, but as has been said and must be oft repeated, both cannot multiply and replenish their kind under ex-host conditions. That is a critical difference! That is the only difference of moment between an obligatory and facultative parasite. Why thrash this same old straw over so much? Scarcely one of the text-books on infectious diseases and bacteriology has ever expressed a clear and definite opinion on this point; or if it has, it is the erroneous one that facultative parasitism has reference to ex-host life, but as the microorganisms referred to live in the earth, and not at its cost in a parasitic sense, how can the word facultative be used to refer to the ex-host life? Before me is one of the most modern text-books on bacteriology and infectious diseases, to which most teachers would refer students as an authority. We turn to it and read regarding the origin of anthrax, that "as every outbreak is the result of the introduction into the system of the bacilli, the question naturally arises, How are they introduced on a farm? Where do they come from?" To these questions in regard to the best known of all microorganismal diseases, some kind of a positive answer should be expected. But we are told merely that "the bacteria may get into the soil (!) and may remain there in a dormant state for many years," and that is every word that is said in answer to the questions on the origin of anthrax. Origin and extension are not identical in theory or practice, though often so treated.

Our author absolutely ignores his own question, Where did they, the bacilli, come from? The inference is from a diseased animal, but where did the diseased animal get them? "From a diseased animal?" It may have become infested in a locality; whence came the bacilli to the locality? "From a diseased animal again?" Then if both diseased animal and infested locality derive the infecting microorganism from a diseased animal, what is the difference between an endogenous and an exogenous disease? Does it rest in that little yet mighty word "can"? True, it is a mighty difference. But if the outside locality is sown with germs by a diseased animal, and the disease can also be maintained in indefinite extension if conditions are favorable for its transmission from diseased to healthy animals without the interpolation of the "outside" condition, in what does an

exogenetic disease differ from an endogenetic? Is it in that little fact that the parasite "can live outside the body"? By no means. It is that that "outside" is the natural home of the parasite, where it "multiplies and replenishes" its kind, and the occasionally infested animal organism is the foreign country into which the parasite migrates and sojourns for a while.

One of the most difficult things to demonstrate satisfactorily is that which should be self-evident to all. To make exogenesis and facultative parasitism as plain as possible, let us take a microorganism over which there can be no dispute as to its ex-host life; nor of which it can be asserted that the ground is necessarily infested by or from diseased animals. The question of transmission from diseased to healthy animals does not exist in any direct or "contagious" sense. Nevertheless, it might be possible to keep the disease extending indefinitely by artificial inoculation from diseased to healthy animals. Is then tetanus a "contagious disease"? Its bacillus can live ex-host, yet we do not hear any one claiming for it a semi-obligatory existence as one does for anthrax and many other bacilli. Not only can the bacillus of tetanus live outside the diseased body, but that is its general place of abode, whereas the diseased body is only the accidental and rare one. Why this difference between bacillus anthracis and tetani? It is mostly to be sought in the fact that one is aërobic and the other anaërobic. The one can easily fix itself, develop and multiply, whereas it is no such easy matter for the other to find the conditions suitable to its existence. Considering that the exposure to the bacillus of tetanus is almost constant in comparison to that to the bacillus anthracis, it would be interesting, if not valuable, to know why infection is so infrequent. The absolute necessity of some clearly defined use of language and of dropping the word contagious entirely from use, is to be found in the recent literature of Asiatic cholera, a disease unequivocally without contagiousness, and an exogenous disease of the most marked type caused by a decidedly facultative parasite. Notwithstanding all this, the books are full of the contagiousness of Asiatic cholera.

The memory of the late outbreak in Hamburg is still quite fresh in mind. It is noted for the striking exemption from "contagion" of those most exposed (that is, in the thick of the battle), the physicians, nurses, and official hygienic corps, not one of whom died, and scarcely one was at all ill of cholera; and this in an outbreak with some twenty thousand cases and ten thousand deaths. To be sure, the ex-host life of the comma bacillus has not been proven, but does any one doubt that this microorganism finds its general habitat in the soil of suitable localities and is exceptional in man?

There is a law of parasitic pathogenesis in relation to infectious diseases which requires most diligent investigation to demonstrate it to the people as well as the profession. It is this: Saprophytic germs once harmless and living as natural inhabitants of a virgin soil frequently become pathogenic when that soil has been saturated for years, or to a sufficient amount, with the excretions of animal life, and, primarily, in that species of animal life which has polluted the soil. Such diseases might be called the penalties of ignorance in the process of civilization.

Nothing more fully illustrates this than some of the infectious diseases of our domestic animals, particularly the horse. The so-called spinal meningitis of the horse is a "new disease," which grows less and less frequent the farther we go west and the more recent the settlement of the country. Again, there are diseases of locality, in the sense of primary origin, just as much as there are diseases of species. Asiatic cholera, anthrax, tetanus, yellow fever, typhoid fever, and diphtheria are diseases of locality, just as measles, mumps, scarlet fever, syphilis, glanders, infectious pleuropneumonia, and rabies are primarily diseases of species.

The majority if not all of the facultative germ parasites are saprophytic. They live in and take part in the processes of decaying vegetable matter. Some of these microorganisms are pathogenic in animals in exactly the condition they are in their outside home without the aid of any polluting excreta of animal origin in the soil. Tetanus is surely an example of this primitive natural pathogenetic energy in a microorganism. Many aboriginal people, such as those of the Solomon and other islands, who use poisoned arrows in war or chase, charge these arrows with dirt containing the tetanus germs, the dirt being the ordinary abiding place of these microorganisms. Another point is that the manure of horses that are perfectly well often contains the tetanus bacilli. From whence do the horses get them—from other horses? Here is a point which tetanus shares in common with anthrax and all facultative microorganisms. The horse and other animals may take the microorganism into itself with food or water, and, whether disease is caused or not, again give up the germ to its native soil, thus fulfilling the law, "from the ground didst thou come; unto the ground shalt thou return." The only reason the tetanus germ does not cause disease when taken in with food is that the conditions are not suitable. It is sufficiently pathogenic under favorable intra-host conditions, as numerous experiments with such materials have shown. Wherein, then, lies the difference between the bacillus of tetanus and that of anthrax? Do they not both deport themselves exactly alike? Are they not both saprophytes

which can become pathogenic under favorable conditions? Do they not both live out most of their lives in the soil? What grounds are there then for inferring that they are parasitic most of the time, as all the authorities either actually do, or tend to teach, as if the life "outside the body" was the rare condition, and the faculty of living ex-host, something the microorganisms "can" assume at pleasure? If so, then the term "facultative parasites" is erroneous, unless the earth be considered a host, at the expense of which the microorganism lives. Then all is parasitic. But it is not in this sense that parasitism is considered.

Another fact in the life history of tetanus and anthrax is apparently this: The naturally pathogenic saprophytes that live and thrive amidst decaying vegetation are generally virulently pathogenic in herbivora, in omnivora somewhat, and in carnivora only slightly so, or not at all. On the other hand, the "civilized" saprophytes seem to owe their pathogeneity to animal pollution of the soil and are more directly pathogenic in the polluting species, as previously remarked. If this has more value than a mere hypothesis, yellow fever and Asiatic cholera, like typhoid fever, must be classed as "civilized saprophytes," which may or may not be naturally pathogenic according to the amount of animal pollution in the soil, while such microorganisms as tetanus or anthrax may or may not be pathogenic, according to the concentration of the chemical constituents of decayed vegetable life in the soil of their native heaths.

Anthrax not Malarial.

It was the opinion of many of the ablest observers prior to the natal day of the bacterial age that anthrax was a malarial disease, a "malarial neurosis" to speak with Heusinger; hence we read much of anthrax malaria and the miasma of anthrax. The same terms and ideas pervade many modern books, more especially those of a practical nature. Applied to anthrax they are meaningless. The use of the word malaria, or miasma, in the historical sense, simply implied the local production of a poison polluting the air. A miasma must be gaseous. It was not something suspended in the air, but a something which was an inseparable part of the air. In that sense we can still speak of a poisonous miasma. A miasma has none of the characteristics of a germ inficiens. It is something produced, but not something which can reproduce itself *ad infinitum*. Hence the much vaunted "anthrax poison" which impregnated soil and atmosphere was simply like all other myths, an hypothesis of ignorance, for no poison can reproduce itself. As shown in the article on glanders,

the mythical volatile malaria of pre-bacterial days has finally acquired a fixed nature, and a malarial disease is now one, the cause of which lives in a locality, infests susceptible forms of animal life *when there*, but the infested animals cannot directly or indirectly transmit the disease to other animals, and though they may be still diseased and leave the primary malarial centre, still they cannot transmit the pathogenic *ens* to any new locality. In other words, malarial infection is fixed both in locality and the infested individual. How different it is with anthrax! The only thing it has in common with a malarial disease is in locus of primary origin. It is local in origin. On the other hand, the diseased individual is a source of possible danger to others while living; and when dead, the disease can be transmitted from it to other individuals, and the diseased individual may be the means of extending the disease to secondary localities.

Anthrax a Local Disease.

That anthrax is invariably a locality disease has been indicated above. So much is universally accepted. No matter how widespread an outbreak may appear, an analytical study of its nature will reveal the fact that in no case is it an epizootic, but rather an apparent epizootic made up of individual enzootic eruptions. The most extended outbreaks illustrate this fact the most clearly. The most malignant and dreaded centres of disease may be in the midst of an entirely unaffected country, an oasis of death and destruction in the midst of a garden of health and prosperity. Such pestiferous centres have been known almost as long as the localities have had a history, and are known as "anthrax districts." Whether or not there are many such in this country we do not definitely know. The government takes no means to find out. That they exist in Europe is well known. In this connection comes up a most interesting question: If the bacillus of anthrax is only one that *can* live outside the body of the diseased, and the disease is only spread by the diseased animal, how did the first animal become diseased, and how is it the disease got to this country when its nature is such that no animal could live to bring it across the waters? There are districts in which anthrax prevails in the valley of the Mississippi, and in all our Western prairie States. I have seen isolated outbreaks ("sporadic," they call them) in Nebraska, in which "the oldest inhabitant" had no idea of anything having died in the vicinity and been buried, but of course they cannot say that buffaloes had not perished there in previous years. If so, from whence did those animals acquire the bacilli?

The regular, historical, "chronic anthrax districts," which extend to a time beyond that to which the memory of man runneth, are generally marked by a very profuse vegetation, with which is naturally connected a generous amount of moisture in comparison with the surrounding country. The general description in the books, that land must necessarily be boggy and the vegetation something tropical in its profuse luxuriance, is liable to be misleading to those who have not had considerable personal experience. The description must be taken invariably as comparative in relation to surroundings. In point of fact, it never means bogs or places continually moist to the surface. There is no anthrax in such. One necessity to anthrax is the condition of drying out and yet retaining moisture in comparison to surroundings. If in place of "bogs" our authorities would say places liable to be flooded but drying out to a considerable degree in summer, and often exposed to the full action of the summer's sun and protected from cooling winds, they would describe an ideal "anthrax centre." In our prairie States, some of the most marked centres are "cups" in the high prairie-lands, which are more or less full of stagnant water from the spring rains, while the surrounding prairie is generally parched and dry in August and September. The only green verdure is frequently the grass about these cups, and it is among the roots of this grass that the bacilli live. It must be remembered that bacilli are not found very deep in the soil, there being nothing there for them to live on. One of the most malignant anthrax centres in the world is the top of a very high hill, often called a mountain, which no one who did not know it would ever suspect it of having been "sure death" to cattle for years as soon as the summer heat had dried it out sufficiently in August. When the sides of this and the surrounding hills, as well as much of the valley land, is dry and the grass hard and poor, this hill top strikes the eye from the distance as a beautiful dome of green velvety verdure. A careful study of the topographical geology of this hill top reveals a regular basin, the base of which is hard, impervious rock, the cavity being filled with the finest and richest of loam, the accumulation of ages. In the spring this basin fills with water, the surplus running out at lower places as small streams down the sides, which has led the people to assume the existence of springs. None such exist. With the cessation of the spring rains the overflow of water ceases, and as the sun comes farther north the surface dries and the grass begins to grow. In August the ground has become hot enough for active development of the bacilli; then woe betide the bovine that is unfortunate enough to break through the fence enclosing this beautiful yet pestiferous ›ak. There is no question that to cut down and into the stony sides

of the basin beneath the level of its deepest point would give such drainage as to make an end of it as an anthrax centre in a very few years. Similar localities are also the seat of an anthracoid disease once embraced in the anthrax group, emphysema infectiosum, or black leg. What experience the writer has had with these diseases has been almost entirely in such localities as those just described; that is, in moist places in high lands, and only once in land that was subject to spring overflow; never in bogs or swamp-like lands, where the water invariably approached the surface. How did anthrax get to such a place as the top of the hill described? In that case it seems as if it must have been due to an animal infested elsewhere (the whole region of the lower Alps is replete in anthrax and black-leg centres, though becoming less with cultivation and drainage), which must have worked its way up there and died in times past and left the seeds of death for future generations of cattle.

The conditions essential to an anthrax centre are: (1) Bacillus anthracis; (2) a rich soil with a sufficiency of moisture; (3) profuse vegetation and rapid decay of the same; (4) a suitable temperature of the soil.

If it is true of the animal "no bacillus, no disease," it is equally true of the soil in regard to anthrax. If it is true of the animal, no infection unless it offers a suitable feeding-ground to the microorganism, it is equally true of the soil that unless it supplies suitable chemical and physical conditions the germ cannot live in it, or if it lives, it is not pathogenic.

In looking over the literature of this subject, one will find that many modern books have continued the erroneous language of an earlier date, when men knew there was something in the soil of a locality, something deadly, but what they knew not, so they called it a poison and spoke of "anthrax poison." A sharp line must be drawn between the bacillus *per se* and its product. The bacillus or its spore may be and must be in certain localities all the year round, and yet for the major part of the time the locality is perfectly safe. The poison producer is in the soil, but it certainly produces no poison that is deadly to animals grazing on it at this time. It is only when it multiplies and the roots of the herbage are surrounded by the germs that grazing animals either take them into it with the food, or they gain access to slight abrasions of the skin, which would seem to be the most common mode of invasion.

It is also possible that a certain microorganism can pervade the soil of a locality and be pathogenic to animals grazing on that locality only when its surface soil offers certain specific chemical conditions for the microorganisms to live in. If the virulence of micro-

organisms can be mitigated or removed, or lost in certain methods of cultivation in the laboratory; if certain varieties lose in virulence, or gain it, in certain animals, is it not only a rational but a necessary assumption to suppose the same things occur in the ex-host life of facultative parasites? Practical observation is all on that side of the question. It is a fundamental experience that the local eruption of anthrax is inseparably connected with the highest temperature of summer, and occurs only after the surface soil has become thoroughly warmed, and that a certain degree of moisture is necessary. Too much water is just as much against the pathogenic development of the bacilli and spores as too little. August and September are the favorite months for the virulent development of the bacillus of anthrax and that of its colleague, the bacillus of infectious emphysema or black leg.

The question has been lately asked, though answered only in one way: Is it necessary that a soil be impregnated with bacillus anthracis, or is it also able to generate the microorganism spontaneously?

Spontaneous generation is pure nihilism and out of date. Regarding the soil being impregnated with the bacilli, the question is badly put—unless we interpret it: Are the bacilli, like seed, sown in the soil? This is a comprehensive question. It has been touched once or twice as the swallow flits over the surface of a mill pond. It embraces questions that cannot be answered, such as the origin of microorganisms, and exactly how it is that but an infinitesimal fraction of the various species is pathogenic in animal life. One thing is safe to assume, and that is that the earth and water in some such form as at present must have anticipated the development of all life, including microorganismal or bacterial, as the very earliest of all representative forms. Such simple organisms do not give grounds for assuming much change in their manner of life since their first development. Therefore, it is probably true that the earth, the soil, became "impregnated," but that does not mean by an act of any other form of life than the microorganisms themselves. There is much evidence of a circumstantial nature in favor of such "original" impregnation of certain localities with anthrax bacilli. May it not be that such localities more or less truly represent the conditions primarily favorable to this form of germ life, or at least modifications of those primitive conditions to which the bacilli have adapted themselves? We have no evidence against the assumption, and much in favor of it, that anthrax bacilli find in such "native heaths" conditions favorable to their pathogenetic action immediately on their gaining access to suitable hosts. There are many and serious objections to

looking upon original localities as simply "intermediate bearers" of the bacilli. If that is not so, as it must be admitted it is not in secondary land-infection from diseased animals, then the animal host must have preceded both the earth and the bacilli in the order of evolution. There is no way out of that dilemma, except the other horn. It must have been either animal life, bacilli, earth, or earth, bacilli, animal life. It makes no difference what the course of events may be at present. It is vastly different in regard to primitive conditions.

The question is, How much or to what degree has bacillus anthracis become an obligatory-infectious parasite? Is it so at all? Those who say that exogenous parasites are such as "can" live ex-host, must affirm that bacillus anthracis is almost exclusively an obligatory parasite, which "impregnates" the soil only when sown there by a diseased animal or by the carcass of a dead one. On the other hand, there are anthrax centres in Germany so carefully under government inspection that no animal has died on them for years, and yet when the season comes round they are still liable to be dangerous to grazing animals. It has hardly been claimed that a regularly known anthrax centre has to be "re-salted" each year by the burial of a diseased animal, in order to keep the yield of germs up to the demands of the market. That secondary centres can be made is well known. They would not have much permanency were not the soil the germs' natural home. In one of our prosperous Western cities, on the banks of a large stream, the town cows began to die in rather an alarming manner some years since—one to-day, another to-morrow, then several at about the same time, then a lapse of some days. In this way a goodly number died. The local authorities guessed and guessed and guessed wrongly. On being sent for, the bacteriopathologist of another State at once found it was only the cows of one quarter of the city that had been attacked, and that, dividing the city into almost equal quarters, the cows of each quarter went out to the grazing grounds by a special path and came back by the same. It was in August and correspondingly hot and very dry. On following the path taken by the cows of the afflicted section, it was found that, instead of going out on to the dry dusty prairie as did the rest of the cows, these cattle turned aside from the regular path and went between two bluffs and by a narrow path down on to the banks of the river, where was a splendid piece of flat grazing-ground, with an abundant supply of water in the subsoil. This place was covered with mounds, and on inquiry it was found to be the burial-place for all dead animals. Putting up bars before the path between the bluffs put an end to the outbreak. The disease was anthrax. The diagnosis was made ere a sick animal was seen or

examined. The bacilli were found in the manure of the first sick animal at a time they could not be found in a microscopical examination of the blood, though they appeared later. Such a place as that is liable to become a permanent anthrax centre. On the contrary, if an animal dies of anthrax on or is buried in high dry ground, with a gravelly subsoil, though there might be danger for a time, it would not continue; there would not be constancy enough in the degree of moisture, and the frequent changes in moisture owing to rains and dry spells would be disadvantageous even to the spore-bearing bacillus anthracis. It would perish in a few years from natural causes. Constancy of condition is essential even to spores retaining their vitality. Nothing is more opposed to it, so far as natural changes are concerned, than repeated changes from wet to dry of an excessive degree and considerable extent. From 1876 to 1893 the writer had some spores of a culture of bacillus anthracis dried on ligature silk and kept in an ordinary test tube plugged with cotton. They had been subject to no other changes than those of temperature in an ordinary workroom throughout the year. During these seventeen years the threads were tested several times by placing a small piece of the silk under the skin of a rabbit, each time with a fatal result, cultures of bacillus anthracis being made from the rabbit's blood and organs. The last test was in 1893. With a spore-bearing bacillus like that of anthrax there is no reason to doubt the existence of permanently infected districts without the necessity of recharging through the agency of deceased animals. The life of bacillus anthracis is still predominantly ex-host, and only accidentally is it a facultative parasite. Continued transmission from animal to animal to any protracted degree seldom if ever occurs. Except where the animal dies on the "anthrax centre," which is rare in civilized countries, or is there buried, most of the recharging of such centres must be from one or two diseased animals through their manure. In general the animals are driven from such centres ere they die, and no more are allowed to graze there that season. It is also a fact that the most noted centres can be safely grazed on, in the temperate zones, up to and considerably into July with absolute safety, while from the middle of July to October they are often dangerous. So well is this phenomenon recognized in the Bavarian Alps and Switzerland that the people know almost to a day how long they dare let cattle graze on the anthrax districts before they must remove them. Neglect of this experience has often been followed by the loss of valuable cattle. No flood but a sufficiency of moisture in the soil plus the extreme of summer heat are among the most essential factors to the rapid proliferation of bacillus anthracis, if present. The moist-

ure can be maintained in one of two ways: either the locality represents the flat shores of a stream, the waters of which have fallen sufficiently during the summer; or the locality is low in comparison to its immediate surroundings and has a clay subsoil impervious to water and hence no drainage, or it may be a stony basin as previously described. Saprophytic germs, like the vegetation they thrive among, require a certain amount of moisture to develop; otherwise the vegetation would not grow and decay fast enough to answer the demands of the microorganisms. Not the microorganisms in the first instance, but the effects of the struggle for existence in the rapidly growing vegetation, is the condition essential to their saprophytic life, and in many cases—if not all—to their pathogenic property in animal life.

As intimated previously, neither bacillus anthracis nor any other saprophytic microorganism multiplies and replenishes the earth for any length of time if that earth be sandy, rocky, or dry. The parable of the seed falling on stony ground is as applicable to microorganisms as any other seed. The richest alluvium is none too good for the saprophytes. Very pathogenic saprophytes may and probably do lose in virulence in dry, well-drained soils; they may continue to live as dormant spores, but fail to multiply under the same conditions. Some of the factors at work under such conditions must be that the vegetation is not so profuse and does not crowd so hard, the struggle is less severe, death of the vegetation and decay take place in no such degree in a dry soil; the germs must therefore lack both food and the necessary conditions to rapid development, or the lack of moisture may prevent certain forms of decomposition, the results of which are essential food to germ pathogenesis. If the subsoil is porous and the rainfall heavy, even though the temperature may be conformable, is it not supposable that the chemical products of vegetation decomposition may be so rapidly washed away as to be insufficient to the pathogenic state of the germs? If the subsoil is impervious the water accumulates so fast as to dilute these products so much that the same effect takes place and the germs are harmless, while they may develop rapidly. It is well known that in seasons of extreme and protracted drought, as well as in seasons of long and protracted rains with complete saturation of the soil, very noted anthrax districts can be grazed upon with safety, which contradicts the "bog" theory for such districts. It is when they are most decidedly boggy that they are the safest. On the contrary, with the ordinary cessation of the rainfall as the hot months approach, and the evaporation of the moisture in the soil, a profuse development and decomposition of the vegetation take place with a rapid multiplication of bacilli of

an ultra degree of malignancy to animals grazing on such places. If this is not all in favor of an exogenous life and facultative parasitism of a most temporary nature, it would be hard to find more favorable evidence.

Transmissibility of Anthrax.

Is anthrax contagious or not contagious? The misuse of the word contagious cannot be better illustrated than in the following: "The chief source of anthrax is contagion. This, however, is seldom direct. Consequently anthrax is not contagious like smallpox. The specific poison of anthrax is transmissible in a high degree. Anthrax is not contagious in the ordinary sense, since an immediate contagion from animal to animal has hardly been proven. It is, however, in a high degree transmissible. The anthrax poison may be preserved for a long time and transported by numerous immediate objects. The poison, which although a fixed one, is also diffused through the air, most often enters the body through the lungs, but perhaps it also gets in with the food and drink."

If anthrax is not contagious like smallpox then anthrax is not contagious at all. An anthrax diseased individual is not necessarily an iota more dangerous to the healthy as an individual than one diseased with tetanus, or a perfectly healthy one. The absolute incorrectness of using the word contagious in the sense of transmissibility and not in its classical sense of primary origin could not be made more apparent. Anthrax is spread by an inficiens, a living entity, but not by any direct act of, or directly from, the diseased. Some persons are frightened to death at the very name of a bacterium, but men of sense are not. Personally, the writer has never given a thought to the dangerous nature of the disease an individual died of, though his life has been spent in the study of infections. With no wounds on one's hands there is no more danger of making an autopsy on a case of anthrax than in cutting up a "beef critter." On the other hand, the body of the anthrax diseased animal is a storage battery of disease and death if not handled carefully. The few statistics from Massachusetts and the city of New York, previously given (see p. 400), show anthrax to be infinitely more dangerous to man than glanders, and probably than any other disease of our domestic animals to which man is exposed. While the blood is often (apparently) microscopically free from bacilli until towards the termination of the disease, it is still a most dangerous fluid. While it is said the bacilli as rods are destroyed in the stomach, it is certain spores are not, and equally certain that the bacilli can be found in the fæces of every anthrax patient, no matter how infected.

Anthrax and Glanders Compared.

Let us test this question of contagion by a comparative study of these two diseases. We will suppose "A" to be a farmer. On one side of his stable he has ten horses, on the other ten cows. On a morning in August his herdsman comes to him and says one of the cows came in sick from the pasture last night. A little later the groom tells him "that horse, 'Jerry,' you drove over to Blanktown some time since does not seem well. He is all off and has a nasty running from the nose, and several of the other horses are in about the same fix." "A" sends for a veterinarian, who diagnoses glanders in the horses and anthrax in the cow. He says to "A," "Where have you driven lately? Have you put up any one's horse of late?" In other words, he seeks a sick horse as the cause of the glanders. He says the other horses must have caught it from the first one, and could he trace it back two thousand years it would be an uninterrupted record of sick horses, even though indirect transmission or stable infection may have occurred in many cases. The sick horse caused it all. Bacillus mallei has no other home. It "can" live for a short time in stables, litter, etc., but it cannot thrive and multiply. We know of no other home for this microorganism than the sick horse. While they are talking over the horse business the herdsman says, "There are two more cows that look sick." So they go over to the cows. The diagnosis is anthrax. The first thing our veterinarian says is: "Shut those windows! In some way you must get rid of those flies, or protect these cows from being stung. A fly lighting on a diseased cow and sucking its blood and then on a healthy one can transmit the disease. Anthrax is far more easily transmissible than glanders." Here is contagiousness enough, and yet were it not for the flies, that sick cow could remain there with perfect safety to the other cattle, whereas the glandered horse is a source of constant danger to the other horses. But the veterinarian does not ask: "Have you bought any new cows lately, or where have you driven? but where are these cows pastured? Did you lose any cows within a few years? Where are they buried? Have you any moist places in your pastures? Any standing water?" He says: "Fence off those places; drain and fill them in." He does not have to wait long to kill the diseased cattle. Nature takes care of that. He kills the diseased horses and orders them buried with no great precautions, and is perfectly certain there will be no more danger from them. He feels safe that a good cleaning and white-washing of the stalls will make the horse stable safe. How different with anthrax! Not a particle of manure from the diseased must be lost sight

of. It must be burned up. The disinfection of the place where the sick cattle stood cannot be too detailed or exact. The sick animals, if killed, must be put away, so that not a drop of blood, or manure, or urine, can fall on the surface of the ground or the stable floor. The bodies must be burned to a crisp. Every particle of blood, every fragment of an organ, if undestroyed, can sow the seeds of disease again in the soil. In other words, *the disease came from the ground; to prevent its continuance its seed must not again gain access to the ground.* In glanders the seed came from a horse, and care must be taken it does not spread to fresh equine soil. Both are transmissible by inoculation from the diseased to the healthy, but those who know both have far less fear in handling a case of glanders than one of anthrax. There the likeness ends. Glanders is a contagious disease. It originates in and extends only by contact with a diseased horse. Anthrax is not contagious and originates only in certain localities and under certain conditions. The anthrax diseased animal bears the same relation to a suitable soil that a glanders diseased horse does to a well horse. The soil is the home nursery for bacillus anthracis, while the horse is the constant home of the bacillus of glanders. In anthrax the infected animal is a temporary intervener for the transmission of the germ from locality to locality. In glanders the stream is continuous in the horse, though the bacillus may stop over at certain stations under certain conditions until the next horse comes along. If the means for transmission were constantly present and active, anthrax could be carried on in susceptible animals so long as the animals lasted, but the original infested locality would probably outlast the cattle. It is a difference with a difference, but a mighty big one when considered in the only true sense of classification, the primary etiological and not that of accidental transmission.

Anthrax Centres.

Summed up, the source of anthrax infection may be stated as follows: Source of primary location and general development of the bacilli, favorable territorial localities; source of primary infection and means of general extension either to other animals or to other localities, the grazing herbivora and materials derived from them, sick or dead. A further means of extension is the washing of flooded streams over places where the bacilli have a permanent abode, primary anthrax centres, or where diseased animals have died or been buried. Secondary anthrax centres are caused by fragments of earth containing the germs and the latter being washed away and landed at favorable localities along the course where other centres of danger may be pro-

duced. Other dispersors of the disease may be wild animals which feed on the carcasses of animals that have perished from anthrax, under domestic conditions dogs, and, in our western States, wolves. Every fragment of an anthrax diseased animal carried away from it and dropped elsewhere may lead to the development of a centre of danger to grazing animals, should the fragment fall in soil favorable to the development of the bacilli. The permanency of such a secondary or tertiary centre of invasion will depend on the character of the soil. Vegetables, especially roots raised on soil where animals that have perished from anthrax have been buried, have been the cause of the disease at most unseasonable times (midwinter), so that every other disease might be suspected before anthrax. By means of the commercial portions of diseased animals, especially where they die in great numbers as they do in Southern Russia (1864, seventy-two thousand horses; 1867–70, fifty-six thousand horses, cattle, and sheep), and Siberia, where the standard articles of traffic are animal products, hides, and hair, anthrax may be carried to any portion of the world. The tenacity of bacillus anthracis, in spore form, has been well illustrated by the threads of silk dipped in a spore culture which the writer kept for seventeen years, and which when last tested in rabbits were still as virulent as ever. No one has any means of controlling the time since the animal died in many cases of wool or curled-hair infection. The following case is of a practical nature, illustrating both the virulence and the tenacity of bacillus anthracis: "The skin of an ox, from the flesh of which two people derived malignant pustule, which died of anthrax in 1852, was soaked in the water of a pond the following year and then made by a saddler into harness. The saddler had a carbuncle. From a flock of sheep washed in the pond some four weeks later twenty perished in a few days of anthrax; horses wearing the new harness made from the hide were infected the fourth day after wearing it and died in forty-eight hours." Dried blood from anthrax diseased animal has been found virulent nearly two years after the death of the animal.

Mode of Invasion.

Having discussed the life of bacillus anthracis so far as we know anything about it and its manner of dispersion over a country or district, it now devolves upon us to consider that parasite in the invaded organism—the host—beginning with the modes of invasion or the ways it gets there. In anthrax as in all other exogenous diseases we have but three common atria for invasion: (1) the respiratory tract; (2) the digestive tract; (3) the cutis, through abrasions or wounds.

Invasion by the Respiratory Tract.

They have been mentioned in an inverse ratio to their dignity as etiological factors in anthrax. It will be remembered that many speak of "the poison, although a fixed one, as often diffused through the air and most often entering the body through the lungs." We are also told that being "small and light, the bacilli are wafted by the breeze, and either directly breathed in by the animal or they fall upon the fluid or solid food and with it enter the body. Such bacterial germs suspended in the air may be washed down by rain, conveyed to a distance, and deposited in any place whither chance may carry them."

It will be only a chance invasion that happens in such a way. Let us consider this air extension and aspiration-invasion a little more attentively than our predecessors appear to have done. The natural home of bacillus anthracis is admitted to be the localities in which there is a stand of water sufficiently high and constant to insure prolific growth of the vegetation. From such a locality bacilli could only be taken up and wafted by the breezes when by some unusual interference with the prevailing order of things the stand of the water had been so materially lowered as to change the conditions previously existing to those of an intense and prolonged drought. Such a thing "can" happen, but it would be about as unusual as an obligatory parasite becoming facultative. Again, if it did, it would be so retardedly progressive as most radically to interfere with the development of the bacilli. There is more "chance" that such a locality would become non-pestiferous, through such drought conditions, than that the germs once there, or still there, would be wafted by the winds hither and thither. Danger of aspiration-invasion of bacillus anthracis from that source may be considered as beyond the range of possibility. The only other telluric source from which there is a chance for bacilli to be taken up by the air and wafted by the breezes into the waiting organism of some kindly disposed herbivora, is from the droppings of diseased animals on the open fields or from a cadaver of the same, or portions thereof, when turned to dust through the action of the sun, the winds, etc. This is possible, but the invasion of a healthy animal from such a source and in such a manner can only be by chance, and a very long chance at that. Aspiration-invasion in anthrax may be well spoken of as "chance infection," even in man, though here the chances are greater. For instance, if wool rags or curled hair happened to have come from anthrax diseased animals and to be full of dust which is stirred up by handling, then the disease would begin as

an aspiration-bronchopneumonia. How many such cases are known to have occurred in animals in which bacillus anthracis was the specific factor? It is a striking illustration of the careless superficiality with which even most competent men express themselves, that the author from whom we have quoted in favor of aspiration-invasion in anthrax does not even mention a lung lesion in his description of the lesions in animals, whereas air invasion would be impossible without such lesions, even in such a peracute disease as anthrax often is. Aspiration-invasion without atelectasis is unthinkable. In acute and subacute cases evidences of bronchopneumonia would certainly be manifest. If we turn to the same authority in reference to anthrax in man we find a like poverty of evidence in favor of aspiration-invasion. In fact we find none. We find nothing indicating bronchopneumonia or atelectasis. On the contrary, we are told that "the lungs, on the whole, are but little changed." Another very high authority says: "Pulmonary anthrax, *the rarest form*, develops in consequence of the inhalation of dust charged with the bacilli or their spores." A modern writer of an accepted text-book tells us: "Wool-sorters' disease is anthrax of the lungs," but four lines farther on the writer says: "Wool sorters engaged in picking wool readily inoculate themselves through a scratch or pimple," which does not necessarily induce lung disease. Aspiration-invasion occurs, however. The necessity of exact statistics in regard to the doorways of infection is an absolute necessity in anthrax, glanders, and all infectious diseases. So far as the evidence has been available it certainly does anything but justify the conclusion that the customary medium of the communication of anthrax is the air, whether the bacilli come out of the soil or from the living animal.

Invasion by the Digestive Tract.

The difficulties in the way of intestinal invasion have been somewhat magnified, and consist mainly in the fact that pure rod cultures without spores are generally destroyed in the stomach, while the spores pass on and are saved to multiply in the intestines and become dispersed over the body. The extreme high limit of temperature for the sporulation of bacillus anthracis is universally given as about the normal temperature of those mammalia in which the disease most often occurs, that is, 37° C. or 98.6° F We do know that a very slight reduction of the normal temperature in the presence of oxygen is followed by most active sporulation. Sporulation has been found in the manure of anthrax diseased cattle as soon as it could be transferred to a slide and examined from the moment it was dropped, the microscope being

on a table within a few feet of the cows. When authors speak of sporulation taking place between 30° and 37° C. they place the lower limit quite too high. How explain the continued existence of anthrax centres "in the farthest inhabited polar regions, Lapland and Siberia," under such conditions? In the earth the average condition must be sporulation and bacillary development from spores. The few examinations that have been made show that.

If it is considered that the time for anthrax devastation is generally the dryest season of the year, when the grasses are dryest and hardest, and the coarse grasses are alone green; further, that the finest grasses in anthrax centres are often to be had only by consuming a lot of coarse, wire-like, saw-edged sedge, it should not be necessary to enter into any very detailed discussion as to whether invasion via the digestive tract is possible if we include the lips and oral cavity in that tract as we must. The bulkiness of the food, the manner in which it is swallowed, especially by ruminants, offers the freest opportunity for ingesting bacilli, as either rods or spores. Again, an absolutely intact lining membrane to the rumen of a ruminant is one of the seven wonders of the world. That infection must take place via the digestive tract is beyond all question. For a long time it was assumed that swine were immune to anthrax, and we do know they have less susceptibility than herbivora and more than carnivora; but it has been found that they are by no means immune to large numbers of the bacilli, if allowed to feed on animals which have perished from anthrax. They also succumb to sizable injections of virulent cultures, but will endure much larger subcutaneous inoculations than injections into the abdominal cavity. Some very contradictory evidence exists in regard to the consumption of beef from the carcasses of anthrax diseased cattle. A whole community of a small locality has frequently eaten the beef with impunity, while those who skinned the animal died. It must be remembered that wounds or slight epidermic abrasions are far less frequent in man than in grazing animals, and again that most of the cases of this kind have been in Germany, where if they do eat raw salted pork they have a corresponding dislike for rare beef, and where the "common folk" seldom if ever enjoy a roast, always eating boiled beef in order to help out with the soup. These things lessen the chances of human intestinal infection in comparison to animal to such a degree as to nullify its value to a great extent. Not denying aspiration-invasion even in animals, and admitting it in man under certain conditions, as well as the greater probability of intestinal infection, all the evidence goes to show that the chief method of invasion in man and beast must be

Invasion by the Injured Cutis or External Erosions or Traumata.

The same author that told us "wool-sorters' disease is anthrax of the lungs," again says: "Another way in which the disease may be communicated may be illustrated by the transmission of the disease to man. Those who handle carcasses, wool, or hides of infected animals are liable to contract the disease. Slight scratches, cuts, bites, and pimples may readily be inoculated by the bacilli or their spores. Veterinary surgeons, butchers, herdsmen, cattle-drovers, in fact all those whose occupation leads them to cut open or skin cattle, sheep, or horses, or to handle hides or wool, are liable to fall victims to this disease." There is probably no microorganism which is more surely pathogenic in the smallest representation (which means that one or a half-dozen may multiply to millions and kill an infested host) than bacillus anthracis. "The injection of a *single* bacillus of anthrax under the skin of a guinea-pig—an extremely susceptible animal—produced death." By "extremely susceptible" is meant nothing more nor less than that the guinea-pig offers a most favorable soil to the pathogenic life of bacillus anthracis. Considering the difference in size, the vastly greater amount of bacillus toxin requisite to cause disease and of bacteria to produce that toxin, and the terrible fatality of anthrax in cattle, horses, and sheep, it is a serious question if the "susceptibility" is really any greater in guinea-pigs than in the larger species. The clinical results of infection certainly favor this conclusion. If a solitary bacillus can do so much in a guinea-pig, is there not some ground to assume that similarly minute infection can take place in animals so exposed to invisible abrasion of the epidermis as the grazing herbivora, and that general infection can occur without the production of a visible local lesion? In this connection it is often said that cattle have a greater disposition to anthrax than horses or sheep. In point of fact, speaking for semi-civilized countries, are not cattle in general infinitely more exposed to superficial abrasions than either horses or sheep? In the first place cattle are grazed in localities far more likely to contain anthrax centres than sheep. Sheep thrive best on dry, stony pastures. More than fifty per cent. more cattle are grazed than horses. Cattle seek out, especially in fly time, the very spots likely to lodge bacillus anthracis. They more easily wound themselves (abrasions) about the lower limbs than other animals. Flies are a most active conveyor of the bacilli where diseased animals exist. Again, the manner in which cattle graze, the tearing off and up of the herbage with the tongue, is far more likely to cause injury of the lips and tongue than is the case in animals provided with upper and low incisors. By

this means bacilli in the dirt about the roots of grasses are more liable to be swallowed by cattle, and get into abrasions about the mouth or in the stomach, than by either horses or sheep. A most remarkably misleading statement is that "horses are less readily infected than cattle, sheep, or goats," because "they can consume with impunity foods which occasion the disease in the others." It is a pity that such bold statements so often occur in medical literature entirely unsupported by facts or theory. One would like to ask what foods? None is mentioned as necessary to be avoided by horse-owners. It would seem as if the reasons horses are *apparently* more exempt than cattle have been given above. They are not grazed so much, and are less inclined to seek and stand in marshy places. They have more delicacy in feeding and drinking, and a different method of grazing. When horses are raised free, as in Russia and Siberia, where anthrax prevails to a more destructive extent than elsewhere, the loss of seventy-two thousand in one year (1864) does not look as if horses could "consume foods with impunity which occasion the disease in cattle, sheep, and goats," the probability being that cattle at least were grazed in the same districts. The proneness of cattle to swallow foreign bodies and thus injure the mucosa of the oral cavity, pharynx, œsophagus, and lining membrane of the first two stomachs is another very active factor in augmenting the susceptibility to anthrax of cattle over other herbivora. The facts, duly considered, certainly point to cutaneous or traumatic invasion as the predominant modes by which bacillus anthracis enters the body of its host.

Etiology of Anthrax in Man.

If anthrax is the most ancient of all known diseases it is none the less widespread over the world, occurring in the northern districts of Lapland and Siberia, in various parts of the temperate zone, under Africa's burning sun, and along the plains of La Plata and the Amazon. It enjoys an equally wide dispersion over the mammalian divisions of the animal kingdom and includes man in its pestiferous embrace. As before noticed, the disposition of the mammalia to anthrax may be expressed in this ratio—herbivora, omnivora, carnivora—the first having the greatest, the last scarcely any susceptibility under natural conditions. Both omnivora and carnivora appear to be absolutely immune to local infection, even when living in notoriously infested districts, frequently drinking the same water and roaming over the same territory in which herbivora may have been infected, and are dying at the time. This fact alone should be

sufficient to nullify the aspiration-infection theory in regard to anthrax in localities of primary location. This exemption of omnivora and carnivora, living in the same localities where herbivora may be perishing of the disease, and a long time noted as "anthrax districts," must not be inconsiderately grasped as direct evidence of less disposition to infection in the former. The question is by no means so simple. While there is no doubt that the omnivora have far less disposition to anthrax than herbivora, it is equally true that the more carnivorous they are the less they have, as shown by feeding experiments in rats and dogs. Still the liability to infection in these species when living in an anthrax district is much less than that of herbivora on account of their manner of life, and because they do not acquire their food by grazing, thereby vastly augmenting the possibility of the bacilli entering the body, as is the case with herbivora. Swine are considerably protected from the microorganisms causing infection through cutaneous erosions or small traumata, the subcutaneous fat tissue offering very poor conditions for the nutrition of the germs unless introduced at once into the lymphatic system and from thence to the blood. As a rule, men are not walking barefoot, nor grubbing with their hands in the soil in anthrax-infected districts. Carnivora have not disposition enough to become infested by traumatic inoculation if exposed in natural districts. The numerical invasion of the bacilli would not be sufficient to insure infection. Reports of the devastations from anthrax in notoriously infested districts might be taken to indicate the invasion of men under the same conditions as susceptible animals. For instance, in the district of Novgorod, Russia, in the four years of 1867 to 1870, fifty-six thousand horses, cattle, and sheep, and five hundred and twenty-eight men are reported to have perished from anthrax. It would be an easy way of getting out of a difficulty to assert that all were infected under, and exposed in the same manner to, the same conditions. Such a conclusion would be unwarranted and erroneous. This becomes evident when it is remembered that in the United States and England the greater number of cases of anthrax in man can be traced directly to the handling of wool, hair, or hides, which have been taken directly from the carcasses of animals that have perished from anthrax. For this reason it is far more in accord with known facts and common sense to assume that the five hundred and twenty-eight cases of anthrax in man in the province of Novgorod were all acquired during the processes of skinning, shearing, or burying the dead animals, and not directly from a common cause present in the locality.

Anthrax a Vocation Disease.

If glanders is a vocation disease in man anthrax is no less so. The same is true of the greater majority of the zoonoses in man. There is not now, and has not been during the historical period, any other source for anthrax in man than direct contact with a diseased animal or indirect acquisition through handling some product of a diseased or dead animal. In this regard man stands in the same relation to the disease as he does in glanders and all infectious animal diseases acquired by him. In this sense there is no difference to man between an endogenetic-obligatory and an exogenetic-facultative parasitic disease of animal life. Man acquires the microorganism either directly or indirectly from a diseased animal. Both classes are contagious and both infectious. There is no differentiation. Nothing could better illustrate the wisdom of the ancients in their differentiation of diseases into contagious and infectious, mystifying as the classification is to most moderns and meaningless, unless we remember that primary origin and not clinical transmission was meant. If we could remove every case of glanders from the country we should make glanders in man impossible after a slight clearing up of stables and utensils. Should the same method be practised in anthrax and every diseased animal be surely burned up and all articles of commerce having such an origin be destroyed, we should have no surety whatever that the dangers of the disease had been removed. In the case of glanders we should have destroyed the locus of primary origin, so far as we know of any, in destroying all diseased horses, and cleaning things liable to be polluted by their discharges. In the case of anthrax we should have left the loci of primary origin, the anthrax districts, untouched and every gate open for the future eruption and extension of the disease. This shows at once that transmissibility gives no scientific basis for the differentiation of parasitic diseases, though it may have a limited clinical value.

Intestinal Infection.

Mycosis intestinalis, or infection from the consumption of anthrax diseased material, is a form of infection which might occasionally give support to the hypothesis of spontaneous generation to those naturally inclined to look in that direction for the genesis of unusual or unsolvable things. In the United States and England this form of anthrax invasion must be very uncommon, still we have experiences enough to be well acquainted with the difficulties of discovering the "guilty person" in putting diseased meat on the market. The buyer

"had no idea it was diseased" until the physician assures him he must have eaten something of the kind. The retailer knows nothing about it. The wholesaler and the butcher are willing to swear any kind of an oath that the meat was all right when it left them and the animal as free from disease as their own dear bodies must assuredly be. Except in the rarest and most desperate conditions the raiser or owner of a diseased animal, no matter what the disease, need not be suspected of consuming its flesh.

How different the conditions among all but the richest of the agricultural classes in Europe, where fresh meat, or meat in any form, is a rare article of food even to those who raise it. From personal experiences, while investigating anthrax in the notorious districts of the Bavarian Alps with Professor Feser of Munich, I have been convinced of the difficulty of making an owner confess that he had cut up and packed away the carcass of an anthrax diseased animal. We would hear of a case of anthrax on a certain farm, and by careful investigation assure ourselves of the fact, but when we come to ask the owner or his family he had never heard of such a thing. "Gott bewahre! Ich habe nie Milzbrand in meinem Vieh gehabt!" And all the women and children, men-servants and maid-servants would say "Ja, das ist wahr." Having police authority and being government officials we would descend into the cellar, accompanied by the officious family, the members of which would bring forward every barrel and vessel but the one containing what we were looking for. Careful and persistent search would generally reveal some freshly dug earth, beneath which would be a freshly salted hide; and in the darkest part of the cellar a barrel of freshly salted meat would also come to light, the origin and nature of which was totally unknown to the Bauer or his family. "Der Teufel muss es gebracht haben," or "ein böser Nachbar muss es hier eingesteckt haben." These people were all the more obstinate because they knew as well as we did that unless they were infected, who cut the animal up, there was little or no danger to those who should eat the flesh if cut in small pieces, well salted and allowed to stand in pickle a month before using.

Medical literature is replete with such cases as this. Of two hundred persons who ate of the cooked flesh of a diseased ox not one became diseased, while five who handled the fresh meat became diseased and three died. Whatever anthrax toxin may be, it certainly is either not dangerous to man if taken into the stomach or is destroyed in the pickling and cooking of the flesh. Were American and English farmers as accustomed to eat such meat as the continental of the same class are, they would be far more likely to acquire anthrax. We might then speak of the "greater disposition" of the poorer class of our

agriculturists to anthrax. Such would not be the case. The truth would be that the continental would not think he could luxuriate in a "rare roast," even if of anthrax origin and given to him, but would boil the meat thoroughly so as to make the most of the soup as well as the meat. Hence the dangers of infection from that source are extremely rare in comparison with the amount of such meat that is actually eaten in the anthrax districts. The sole danger lies in the presence of living spores in the flesh. The same are destroyed when the flesh is properly pickled and also by thorough cooking.

Traumatic Invasion.

Direct inoculation of anthrax in man is not very common. It can only happen in those whose calling brings them into direct and personal contact with the diseased or the dead. There must be either an abrasion of the epidermis or a wound of the skin to insure infection. Direct invasion in anthrax can occur only to the physician, nurse, or undertaker, or some one coming in direct relation with the patients. In this regard physicians sometimes forget their obligations as in the case of a wool-sorter with a malignant pustule in a finger, which the physician operated upon, but gave the wife no caution in regard to handling the dressings, so that she became infected through a fresh cut on the thumb while putting the rags in the fire. The woman died while the husband lived. Physicians have inoculated themselves, as in the case of one who on dressing a malignant pustule carelessly put his hand to his lips where he had an excoriated "cold-sore." Veterinarians and knackers have been more frequently the victims of their own carelessness than physicians, nurses, undertakers, or the regular butcher. In general, direct infection has been very rare in these classes, especially in this country and England, where the number of anthrax-infected animals is not alarmingly great, and such as there are have not value enough to be operated upon, skinned, or cut up.

In making necroscopical examinations of animals which have perished from anthrax in this country, particularly in the South and West, the operator needs to use far more precautions against the strings of flies which swarm about him, and not to expose his arms or face—a veil is an absolute necessity—than he would against a swarm of bees, and the same as he would exercise against cutting himself. How great a part the mosquitos play in the spread of anthrax is not known, but that they do light on and draw blood from animals no one need doubt. There is danger to man from flies where anthrax exists among animals. Rarely, but still possibly, the house-dog might infect a person by licking an abraded portion of the body,

hands, or face, after having made a meal on some anthrax-infested flesh.

Indirect Infection,

Anthrax being a vocation disease, experience shows that in this country and England the percentage of direct infection is practically null in comparison with the disorders following indirect infection, and occurring in those whose vocation brings them into direct contact with natural or preserved materials derived from the carcasses of animals that have succumbed to anthrax. Notorious among these are wool-sorters, curled-hair workers, handlers of sun-dried hides, and rag-sorters.

Here we find two forms of invasion as practically possible. The one is due to the aspiration of the microorganisms—as spores—mixed up with the dust in the rags, hair, or wool; the most infrequent form of infection has already been discussed; the other is due to infection through an abrasion or wound of the cutis, *inoculation proper*. The very nature of the labor of the rag or wool sorter, curled-hair worker, or handler of hides is conducive to sore hands and the formation of atria favorable to the invasion of microorganisms. The handlers of sun-dried hides seem to offer occasional exceptions to the rule in that a number of cases of infection are reported in which the atrium was a razor scratch, or a pimple on the neck or cheek, the scab of which was rubbed off by the edge of the hide owing to the manner in which the men carry them. Anthrax among these classes of operatives need cause no surprise, but the list of cases furnished by the New York City Board of Health, and previously published in the essay on glanders (see p. 400), if reliable, is sufficient to give rise to serious thought (if the percentage of anthrax in comparison to glanders holds for the country), as it shows not only the large extent of anthrax but also a most remarkable extension of the vocations, or rather the possible exposure of many classes to anthrax.

There were sixteen cases of anthrax in New York City from 1888 to 1897 inclusive. Of these two were of unknown occupation. In 1889 four men were reported as "contracting the disease from handling hides." When one reads that one was a laborer he is not surprised, though he fails to see the connection between handling hides and the occupation of "a dry-goods clerk, a boiler-maker, and a carman." Again, in 1890, there were three cases, occurring in "a plumber's apprentice, a laborer, and a musician." These acquired the disease "by handling hair mattresses," but whether they all handled the same mattress or not is not stated, or just what a plumber's apprentice or musician was doing with a mattress to become infected. The same is

true of the laborer. Interest is still further increased by the special mention of the mattress, rather than the hair. Among the others in different years we have a tailor, a mason, and a teacher, who attract attention, though nothing is said as to what they were doing to make the intimate acquaintance of that venomous parasite, bacillus anthracis. The facts show the necessity of the most intelligent coöperation of the health officer, the physician, and the nurse, with the investigators, in order to establish the factors in the etiology of parasitic infections, so that they can be met by the intelligent coöperation of the public and by appropriate legislation far better than what at present exists.

The fact that anthrax in man, in this country and England, is almost exclusively limited to workers in animal products *imported* from other countries, shows that the disease is not only here, but there, more prevalent in that class than in those whose vocations bring them directly in contact with the diseased animals. The dead animal is far more dangerous, when distributed over the world, than the living is to the human beings in its immediate vicinity. The anthrax district, the infected locality, is apparently harmless to man. "Spontaneous anthrax" simply means ignorance of the source of individual infection.

Pulmonary Invasion.

The term "anthracosis pulmonum" having acquired another and classical use in reference to smoke-dust inhalation and the blackish condition of the lungs induced thereby, it is impossible for us to appropriate it for anthrax in the lungs, a seemingly very rare disease, but probably not so infrequent as the literature at command forces us to assume. So far as we have any reliable information, anthrax in the lungs is a peculiarly human complication. There is no reliable evidence that it occurs in animals under the conditions of natural infection. By that it is not meant that there are not disturbances of the lungs in some form in anthrax in animals, for the blood-vessels are often congested; stagnation of the circulation occurs; antecedent chronic pneumonic conditions may be surrounded by those of an acute nature, the indirect results of the anthrax infection; there may be more or less gelatinous infiltration of the loose connective tissue in various parts of the lungs, and hemorrhages here and there, but none of these constitutes anthrax in the lungs in the sense of direct aspiration-invasion, conditions favorable to which scarcely occur in the environments in which animals are exposed to invasion by bacillus anthracis, as has been elsewhere discussed. So far as known it would seem as if metastatic pulmonary anthrax did not, or does not, occur as a complication in either cutaneous or intestinal infection. It is highly

questionable if the aspiration of anthrax bacilli, in a pure and undefiled condition, uncontaminated by dust in any form, causes pneumonic lesions in the lungs in man, though local and general infection may result. It is a fact that in aspiration-invasion in anthrax very few bacilli are to be found in the blood-vessels of the lungs; the collapsed portions, on the contrary, and the lymph spaces, lymph nodes, and glands are replete with them. But in cutaneous or intestinal infection the blood-vessels of the lungs may be found full of bacilli, while none may be in the lung tissue proper or pulmonary lymphatics, except in localities where hemorrhages may have occurred. It must be remembered that in general the course of anthrax in animals is too acute to permit of such metastatic complications in the lungs, and this finds its support in the absence of the bacilli in the blood, until a few hours before death.

According to Eppinger ("Die Hadernkrankheit," Jena, 1894) the rag-sorters' disease does not occur in Germany proper, but is restricted to the paper factories of lower Austria and the Steiermark region. In a general way, though by no means based on infallible evidence, it might be said that anthrax appears in a pulmonary form, as the wool-sorters' disease in England, as the rag-sorters' disease in Austria and the Steiermark region; it occurs as malignant pustule and intestinal anthrax in Germany and some other European countries, while in America and elsewhere, it seems to occur as malignant pustule only. The point desired to lay stress upon is that Eppinger and others who have investigated anthrax as it appears among rag-sorters and wool-sorters, are inclined to the view that in these avocations anthrax invariably appears as a pulmonary infection; no mention is made of malignant pustule ever occurring under the same conditions, which seems as contrary to common sense, as has been otherwise noted, as to assert that anthrax occurs only as malignant pustule in curled-hair workers. There is as much room for dust infection in the latter as for cutaneous invasion among wool and rag workers. Again, the literature gives the impression that the rag-sorters' disease is peculiar to women as women, whereas it is only because women happen to be employed in this department of paper factories. As the two questions here brought up, namely, (1) the specificity of pulmonary anthrax to rag and wool sorters, and the apparent exemption of these latter from cutaneous infection, and (2) the proneness of females to the disease, are of special interest, it may be well to look a little more closely into the nature of the work.

Speaking for the rag-sorters, Eppinger, quoting Schauenstein, says: "The paper manufacturers purchase their rags from whole-

salers, who obtain them from numerous small dealers. The territory from whence they come must necessarily be quite extensive. The wholesale dealers subject the rags to a superficial assorting and cleaning, mostly in reference to quality. The rags are then baled. Most of the rags used in the paper factories of lower Austria and Steiermark come from eastern lands—Hungary and the adjoining countries (notorious anthrax districts). The rags stink outrageously and on this account the bales are opened at the factories in airy, well-ventilated rooms by special employees, where they undergo a form of assortment, the colored being separated from the uncolored, the coarse from the finer pieces, the very dirty, especially bloody pieces, from the cleaner. The last is the special purpose of this assortment. The colored rags are then cooked out in an alkaline solution. The work thus far is done by men.

"The rags are next placed in a storeroom where they may remain for months, the stench not lessening thereby. From here they are taken to the especial assorting-room, according to the demands, where they are cut in small pieces and more particularly separated. For this work only women are employed, and it is in this employment that they are mostly infected with pulmonary anthrax.

"The work of the women is as follows: Each woman has before her a table, by which are movable receptacles for the rags; attached to the top of the table is a scythe-shaped knife standing perpendicularly with the sharp edge from the worker. The pieces of cloth are cut by drawing them stretched between the hands, up and down the blade. Hereby much dust is stirred up as well as in tearing the rags," etc.

The striking fact is that the men who first handle the rags should so generally escape as to cause writers to speak of the induced disease as peculiar to women, and that under such circumstances, with rags containing germs enough to infect through aspiration, there should be no wounded fingers, and malignant pustule should never occur—at least never be spoken of—and anthrax in the lungs should be treated as the only form occurring. One must take this *cum grano salis*. It is against common sense to think that the most difficult form of invasion should occur and the most natural and easy should never find mention. Or is this one of those to be unceasingly condemned cases of organic individualization, which has become so fashionable in pathology, cutaneous infection being left unmentioned though occurring?

There are several peculiarities about this rag-sorters' aspiration anthrax which are worthy of particular attention. One is, that while the nature of the vocation would seem to warrant the assumption that the exposure to infection was more or less constant, that is, that the

bacilli were liable to be in the rags at any time, that the disease seems to occur principally in the spring and fall, at times when catarrhal conditions prevail in the respiratory tract, and only among those in whom it is markedly present. Several are liable to be attacked at about the same time. One may ask: Do the men sorters entirely escape the catarrh, as they seem generally to be able to avoid anthrax infection? Do they escape cutaneous invasion as well? The fact that so many escape out of numerous employees even among the women, and that an occasional foreman, in such a room, has been affected, is strong evidence against the universality of disposition to aspiration-infection, even under common exposure, and the necessity of a local predisposition in the catarrh of the respiratory tubes. That the dust *per se*, irrespective of its contamination with the specific bacilli, is the chief cause of the strictly pneumonic lesion, and somewhat helps to make the bacillary infection possible, is plainly evident from the investigations at hand.

Why is it that we have no reports of anthrax in the lungs among hair-workers, rag sorters, and wool sorters inthe United States; or so few that one finds no reference to them in the special literature on the subject? The terms pulmonary, cutaneous, and intestinal anthrax are most decidedly objectionable as tending to raise to the dignity of specific diseases merely different atria of invasion in a specific disease. In their place we should speak of invasion through the respiratory or intestinal tracts or through a cutaneous lesion; or aspiration, oral, or traumatic invasion.

It must not be assumed that this catarrhal predisposition to pulmonary invasion in rag (and wool?) sorters has any relation to the constitutional disposition to anthrax of man in general. The questions are entirely distinct. On the other hand, given the nature of the organ invaded, its paramount dignity in the human economy, and the specific tendency in anthrax to the development of œdematous conditions in the tissues invaded, it is not surprising that pulmonary invasion leads to a most acute and generally fatal manifestation of anthrax, recovery occurring but seldom. The general duration of pulmonary invasion ere the fatal termination is from two to five days. When the patient survives beyond that period hopes of eventual recovery strengthen as the period continues to lengthen; complete restoration to the *statu quo ante* is invariably a protracted affair. The diagnosis is easy, provided the physician knows the nature of the work of the patients. If there is any discharge (sputum) the bacilli can generally be found in it. As in animals, the bacilli do not appear in the blood of the patient until towards the termination of the disease. That the invasion is, or has been, by aspiration is

shown by the location of the bacilli in the tissues. They are to be found in the mucosa, between the cells, in the ostia of the glands, in the lymph spaces, and in the lymphatics of the trachea and bronchial tubes; within the atelectatic alveoli, and in the lymph spaces of the lungs and the lymphatics, and in lymph nodes along their course. They can and do pass into the pleural cavity through the pulmonary lymphatic system, passing out of it on the surface of the lungs, where they develop and set up a most serious pleuritis with a serous or serosanguineous effusion and often fibrinous exudation attacking the costal and visceral pleuræ. Only after the bacilli have passed the bronchial and mediastinal lymph glands can they get into the general circulation. This indicates why they may be so sparsely present in the blood-vessels while profusely represented in the bronchioles and in the atelectatic tissue and lymphatic system of the lungs.

Aspiration-invasion, or pulmonary anthrax, bears some resemblance to the apoplectic form in cattle and sheep in its almost unannounced explosion, though it is not so spasmodically fatal. The patient may be at work or at home, and appear and feel well, when suddenly a chill overcomes her, and a general feeling of sickness, headache, dizziness, cyanosis of the face and extremities, and vomiting or loss of appetite comes on. Sometimes this is anticipated by a peculiar dry, prickling feeling in the throat. A cough may or may not be present, but as this may be of catarrhal origin it may have little or no value unless the bacilli are present in the expectoration. The temperature is frequently 40° C. (140° F.) soon after the patient is observed to be ill. A collapse temperature may as suddenly appear, and be followed by death. Pleuritic and epigastric pains, precordial pressure, with consequent disturbance of the respiratory phenomena, especially when there are numerous atelectatic, œdematous, or solidifying centres in the lungs, help to make up the clinical picture, which is often added to by excessive cyanosis of the face and lower extremities, the latter being cold; the heart becomes weaker and weaker as well as the patient. The end is generally sudden. The patient remains conscious throughout. Great anxiety seems common to almost all.

Anthrax in the lungs can be said to bear a strong resemblance to primary anthrax in the cutis. In both cases there is a sort of carbunculous disturbance; in both there is marked œdema, more or less hemorrhagic or gelatinous infiltration of the complicated and adjoining parts; in both the bacilli extend over the system by way of the lymphatics; in both the bacilli can directly invade the blood-vessels through the lymphatic system of their walls, and perhaps invade capillaries by passing between their cells when greatly disturbed.

This appears doubtful. Gelatinous infiltrations in various parts of the body are not so common in aspiration-invasion as in cutaneous and intestinal. Pulmonary invasion remains far more a local complication than either of the other forms.

Pulmonary invasion may be said to result especially in an atelectasis, acute bronchopneumonia, œdematous infiltration of the diseased and complicated parts; more or less complete stasis in many larger vessels; pleuritis, which may be fibrinous and adhesive, but more frequently serous and effusive, often on one side and sometimes on both.

Carbunculous disturbance of the nasal mucosa and that of the pharynx, larynx, and trachea with peculiar exudates on the mucosa and circumscribed cellular infiltrations in which the bacilli are plentiful, are not uncommon; hemorrhages along the superior line of the trachea above its bifurcation are frequent. The lymph glands are swollen, œdematous, hemorrhagic, often looking like blueberries, blue grapes, or small blue plums; cross section often shows grayish, medullary centres in a dark blue ground; gelatinous infiltration of the mediastinal tissue is quite frequent. The heart is seriously affected, its muscle being anæmic and fatty; small hemorrhages in its substance are by no means uncommon, and neither is effusion into the pericardial sac. Disturbances of the aortic ventricular valve with demonstration of bacillus anthracis as the cause have been reported and may be an occasional cause of the unusual cardiac disturbances occasionally observed. The spleen is generally tumefied. Catarrh of the respiratory tract is common. Its etiological importance has been alluded to. The kidneys and liver are the seat of the usual parenchymatous disturbances, cloudy swelling, or fatty degeneration of anthrax and kindred acute toxæmic infections; hemorrhages of varying extent in the pia mater cerebri and other parts often complicate the picture.

Pathological Anatomy.

The next question to consider is bacillus anthracis according to its fruits, its effects; the lesions induced by it in the body of its hosts. That anthrax is an infectious disease having generally a most acute course is universally admitted. Tho question is, What kind of an infection is anthrax? Is it a toxæmia or a septicæmia? By the former is meant an infectious disease in which the microorganisms producing the infection do so by remaining local, either at the place of primary entrance or in some organ, where they multiply and produce their toxic product which, via the lymphatics, gains access to the blood. A septicæmia is a disease in which the microorganisms develop in

the blood and give off their pathogenic products directly to the blood. In the end both classes are alike, the blood conveying the toxin over the organism as it does any other material which is added to it. It is a well-known and often disgustingly disappointing fact that during the early hours of a case of anthrax the bacilli cannot be found in the blood drawn locally from the extremities, and that they do not appear until towards the fatal termination of the disease. That a few are in the blood or that they are in it in spore form has long been well known. The terrifically acute progress of the disease sufficiently indicates their presence somewhere. They collect in the organs, where they multiply and replenish their kind, and from whence all their products are added to the circulating stream. In this stage of the disease it certainly is toxæmic in its character and not septicæmic. It probably remains so, as the bacilli in the blood towards the lethal culmination appear to be such as have been crowded out of the organs rather than such as have multiplied in the blood itself. At the *locus invasionis* there is sure to be hyperæmia and engorgement of the vessels, with ecchymoses or more extensive hemorrhages and œdema of the tissues.

Although anthrax presents many pathological conditions, the common property of the majority of the septicæmic or toxæmic diseases still it manifests a few which may be claimed to be peculiar to or pathognomonic of itself. Of these the most striking are the disturbances of the blood by which it is changed into a dark purplish-red, tar-like fluid, owing to the marked destruction of the red blood cells and the so-called "gelatinous infiltrations," always present, and generally extending from and about the *locus invasionis* when such is situated in the cutis or in the walls of the intestines, and between the folds of the mesentery where attached to the intestine, and in other masses of loose connective tissue decidedly vascular, and especially in the capsula adiposa renalis. In no animal is this condition locally more marked than in swine, especially between the jaws and along the inferior portion of the neck when infected from consuming the flesh of an animal dead of anthrax. On the other hand, in no other animal is this condition more widely dispersed over the organism than in the horse. It may be looked upon as pathognomonic, because never wanting to some extent and not present in any such form in any other disease. In animals there is a marked weakness in rigor mortis, especially prominent in the herbivora but less so in omnivora.

The lack of coagulation in the blood is another marked characteristic of anthrax. While common to the disease, the enlarged spleen is in no sense pathognomonic, exactly the same condition occurring in cattle in Texas fever, which long gave rise to the suspicion that

that plague of the cattle in our Southern States was either anthrax or closely related to it; but the thin, claret-wine or dye-like blood of the Southern plague is all sufficient to differentiate it at once from anthrax. Small masses of incompletely jellyfied coagulation float in the fluid of the large vessels and the heart.

The dense parenchymatous organs, liver, kidneys, and heart, often including the body muscles, are more or less anæmic, so far as the parenchyma itself is concerned, clouded, grayish-red in color, sometimes yellowish-gray-red when the disease has had a rather protracted course. On the other hand the veins are engorged, and when the organ is cut across it gives quite the contrary appearance, an excessive amount of blackish-red, thick, viscid blood flowing over the cut surface, especially of the liver, so that one often reads of the liver or the kidney being engorged, which is true of its vessels, but is not true of the active substance of the organ. The lymph glands are invariably swollen, œdematous, and often the seat of petechial, ecchymotic, or diffuse hemorrhage, and vary correspondingly in color. When the invasion has been from a wound or abrasion in the cutis, best seen in man, the lymphatics are often intensely swollen, painful to the touch, and extend as red cords under the surface of the swollen and œdematous skin to the connecting pocket of lymph glands, which are then intensely swollen and often look like purple or purplish-gray plums or grapes in the tissues, as we cut down on them.

The local seat of invasion in man, when situated in the cutis, is remarkably interesting, and may be useful in relation to other animals in which the disease is far less frequently seen during the process of development, especially in the earliest stage. The most minute lesions are the most interesting. The initial lesion frequently appears like an insect bite, with the exception that the swelling is more marked and intensely red, the central point being indicated by a distinct dark-red point, as if the insect had directly punctured a small blood-vessel and a slight hemorrhage had taken place. This spot swells and, becoming pustulous, being filled with a serous, serosanguineous, or hemorrhagic fluid, soon ruptures, leaving a small crater-like opening with a dry dark-red base, over which a scab is formed. The tissues around the primary centre are soon complicated in the embrace of the extending inflammatory processes, diffusely red, and on the confines often surmounted by a row of vesicles somewhat resembling the original, though much smaller. These soon rupture, an eschar covering the whole mass. In the earliest stage numerous bacilli are present in the central point, but as these tissues become necrotic the bacilli approach the confines of the lesion,

where they are present in great numbers. From here they invade the tissues in the vicinity, find their way into the lymphatics, and invade the lymph glands, where they may form small colonies; eventually they gain entrance to the circulation and are distributed over the system; bacterial embolism is common. In man the intensity of the bacterial toxin is especially manifest in the rapidity with which the processes extend into the more profoundly situated subcutis and tissues beyond it, the same being marked by dense infiltration and a mahogony-red color, bands of this color—the lymphatics and superficial veins—extending from it, the whole mass being œdematous.

The veins of the stomach, intestines, and mesentery are in the same engorged condition as those of the rest of the body; the walls of the stomach are often thickened and the seat of punctiform and diffuse hemorrhages; the mucosa is intensely swollen, of a diffuse redness, differing much in shade and itself interrupted by petechial, ecchymotic, and more extensive hemorrhages of a darker color; the mucosa is covered by a thick viscid material; extravasations into the lumen of the stomach and intestines are by no means rare. The mucosa of the duodenum and jejunum is generally affected in a similar manner to that of the stomach, though often to a more intense degree, the hemorrhagic conditions being more extensive; the large intestine suffers in the same way, though less intensely. This redness of the mucosa extends to those of the pharynx and nasal cavity, as well as the mouth. In animals the tongue is not unfrequently the seat of the primary lesion, when it is found in a similar condition—swollen, œdematous, engorged, and the seat of hemorrhages.

The muscle of the heart is invariably swollen and anæmic, and sometimes the seat of small hemorrhages. Serous effusions in the peritoneal cavity and pericardial sac are common. Petechial hemorrhages in the visceral coating of the pericardium, especially at the base of the heart and about the auricles, as well as under the endocardium, are common. In general, the large veins of the lungs suffer with those of the rest of the body, and are intensely engorged; petechial and ecchymotic hemorrhages under the pleura and scattered through the lungs are common. Œdema pulmonum to a varied and sectional extent, according to the disturbances of the circulation, is by no means rare. In primary lung infection the presence of atelectatic centres with more or less intense hemorrhagic disturbance, with a tendency to necrobiotic destruction, is not uncommon; cellular infiltration or actual pneumonic lesions of any extent seldom appear except in direct invasion by aspiration of the bacilli, on account of the acuteness of the malady. Engorgement of the cerebral vessels is present with occasional hemorrhage of limited dimensions into the meninges and a

serous effusion into the ventricles. Hemorrhages in the ovaries and the uterine cavity help fill out the picture.

Symptoms.

In Animals.

The symptomatology of anthrax is not always satisfactory, more especially in protracted cases. The incubation period is very uncertain, but seldom if ever of extreme length. It is dependent on the quantitative and qualitative nature of the invasion. If the bacilli have entered the body in great numbers and at the same time in an excessively virulent condition, the disease may appear like a stormburst out of a clear sky. In such cases it is impossible to speak of a period of incubation. This manner of presentation has been termed *apoplectic anthrax*. Not a suspicion exists that anything is wrong. A personal experience well illustrates its explosive character. During my studies in the Bavarian Alps I approached a woman just beginning to milk a cow, to inquire if there had been any sick cattle on the mountain, or any indications of Milzbrand. The cow at the time was perfectly quiet and apparently undisturbed by anything. Suddenly she dropped on her foreknees, staggered, rose, and fell struggling on her side; a few convulsive kicks and she was dead in almost as short a time as it has taken to write so brief a description. The woman fortunately escaped with no other injury than of her feelings, and the sole stoical remark, "Ja! Ja! Herr Doctor, ich glaube das ist Milzbrand." In such cases there is undoubtedly a period of incubation, but the development of the bacilli is so rapid as to give no time to indicate their presence by premonitory symptoms. In general three or four days must pass by ere indications of disease are present. It is but rarely that the apoplectic form occurs so it can be examined at once, or even that the investigator sees it at all. The lesions are the most extreme blood disturbances, infiltrations, and hemorrhages. In animals local external lesions would seem to be rare.

In the ordinary course of events anthrax takes what may be termed an acute course, though the first disturbances may appear suddenly, such as loss of appetite, often complete; cessation of milk secretion; staring hair, increased respiration, chills, and high fever up to 105° or 107° F.; the extremities are cold; there is often a period of intermittence between the chills and the fever, which once gave rise to the suspicion that anthrax was a malarial disease.

Spasmodic convulsions of the muscles of the body are frequent, while a general twitching of the muscles is still more common. The

animals are very weak, and loath to move; hence they stand isolated when in pasture. The veins of the visible mucosæ are extremely engorged; the membranes are often swollen and diffusely red at the same time. This is especially marked in the rectum, from which are often discharged fæces covered with bloody streaks and hemorrhagic diarrhœal evacuations in which the bacilli are easily to be found. The rapidity with which spore development occurs in such discharges after they leave the animal has been previously noticed. Colic symptoms are very common in horses, but not in other animals. These paroxysms of exacerbation and relaxing in the severity of the attack may continue for several hours, the animal sometimes eating in the interim. In some cases local swellings appear early in the attack, which in reality much resemble those seen in man, except that they are more extensive; these swellings are dense, dough-like, extremely hot, and sometimes so intense is the disturbance that the skin has a diffuse reddish color. Crackling of the skin (like dry parchment), as the hand is passed over these tumefactions with some pressure, does not occur in anthrax, there being no gas development in these local swellings; on the contrary, they are œdematous. It is singular that this error is still printed in some very modern books. The "crackling tumefaction" or sensation is most pathognomonic of a disease once belonging to the anthrax group, but now most decidedly differentiated from it by its baton-shaped bacillus and the lesion spoken of and absence of gelatinous infiltrations, though resembling anthrax in some things, more particularly in occurring at the same season of the year and in the same localities. It is different from anthrax in another marked essential, in that in no disease is there a more marked individual predisposition than in *emphysema infectiosum*, or black-leg.

In the hog the most marked clinical symptom of anthrax is generally the œdematous swollen condition of the tissues of the jaws and under the neck.

In Man.

As in animals so in man the period of incubation is variable from a few hours to several days, though generally longer in man than in the herbivora because of the lesser disposition or less favorable feeding-ground offered the bacilli by the omnivora in general. When the invasion of the bacilli has been by the respiratory tract the symptoms are frequently far from recognizable at once; and the same can be said of infection by the digestive tracts.

The most marked symptoms of local cutaneous infection have already been given in considering the lesions, one of the earliest if not the earliest indication of infection being the "Fliegenstich," or the

papule resembling an insect bite not only in appearance but in its aggravating itching, so that through the patient's scratching a scab is often formed ere the primary pustule has a chance to develop. The continued itching of such a part with the augmentation of the redness and œdematous swelling, the shooting pains in the locality, and the red lines in the skin marking the swollen lymphatics are among the strongest initial symptoms of anthrax. As the disease progresses the hemorrhagic œdematous conditions augment in intensity, and the tissues become more and more discolored and variegated in tints; vesiculation and scab formation over the ruptured vesicles or pustules are decidedly characteristic. Fever is one of the natural accompaniments of such a disease, though not always excessively marked in the early stages. On account of the venous engorgement common to anthrax in all its victims the visible mucosæ are not only injected but often swollen and diffusely discolored; the mouth is dry and the tongue is coated. Cerebral disturbance is frequent. As in animals and in other forms of septicæmia, diarrhœa is frequent. The malignant cases may terminate in from twenty-four to forty-eight hours, and are often preceded by collapse. Not only are the local symptoms more frequent in man than in animals, but they are generally much more marked, slower in development, and enduring longer.

It has been the custom frequently to speak of the local œdema which appears in anthrax aside from that at the point of invasion as forming distinct phenomena, but it simply indicates more general infection or effect of the toxin on the local circulation, and is especially marked in the eyelids and dependent parts of the body, and often gives rise to gangrenous disturbance, "anthrax carbuncle." The local disturbances frequently take an exceedingly mild course, the general infection following the like path though not without disturbing influences in other parts of the body.

The symptoms following the consumption of anthrax-infected flesh are at first those seen in other cases of ptomain poisoning of a like origin—general malaise, headache, gastralgia, debility, weakness, sometimes vomiting, and not exceptionally diarrhœa. If the disease is not fatal in a few hours or within the first twenty-four or forty-eight hours, and time elapses for full development of the bacilli and their generalization over the organism—a kind of metastasis—local disturbances may appear in the form of carbuncles here and there, the favorite localities being along the arm and about the head, progressing in fatal cases to general œdema of the parts, gangrene, collapse, and death. In more protracted cases the general disturbances are still more marked by local œdemas, diarrhœas of a hemorrhagic character, settling of the blood in dependent parts, intense pain, unconscious-

ness, delirium, and accelerated breathing. Hemorrhages from the mouth, nose, and rectum have been remarked in very severe cases.

Diagnosis.

In no case is the bacteriologist's dictum, "No bacillus no disease," more easily applied than in anthrax, with the advantage of an early diagnosis far more in favor of man than animals on account of apparent predominance of local infection and the plainness of the lesions, in which the bacilli can be at once found, whereas in animals they are generally not present in the blood of the superficial veins until towards the end of the attack. In no other disease is a correct history of more importance than in anthrax; in animals, in regard to the nature of the pasture, have there been any previous cases? how did they deport themselves? and above all, though not infallible in its indication, the season of the year is of the greatest importance. The season of the year being between July and October, the symptoms suspicious, the next important question is, Has the locality been an anthrax centre? Were animals buried where this or these animals were pastured? A season of drought following a wet spring should not be forgotten as a valuable aid in a suspicious case. In the winter things are more difficult. Suspecting anthrax, one asks where roots were raised, if fed to cattle, or where the grass was cut. Were there any burials of animals in those fields in previous years?

In man the case is generally far simpler; knowing the business of the person having a local lesion, the diagnosis is often self-evident. Not knowing the business, in case of pulmonary infection, the diagnosis is found with difficulty. In case of meat poisoning in anthrax it is the same until the local lesions begin to appear as in pulmonary glanders, though not so difficult. But in man as in animals in all cases of suspicion and all cases of diarrhœa or blood discharges an examination of the same by the microscope will often bring the diagnosis to a quick solution. It must not be forgotten that the characteristic bacilli are often present in the fæces or sputum long ere they can be found in the blood.

In man the physician generally has the advantage of an immediate examination of the tissues of the local lesion, a drop of blood from which, if properly squeezed out from the depths and not the superficial blood, will invariably contain the bacilli. Inoculation of animals is scarcely ever necessary in these days to make a diagnosis of anthrax.

Prognosis.

The prognosis in anthrax in cattle, sheep, and horses is bad. Treatment at present seems out of the question. The loss is said to be from seventy to eighty per cent. In general, the loss in swine from anthrax is not sufficient to be worthy of consideration. The omnivora having far less disposition to anthrax than the herbivora, the microorganisms remaining for a much longer time confined to their locus of invasion, generalization being consequently much slower, it is evident that the chances for treatment and recovery are exceedingly high in man in all cases of cutaneous infection, the treatment of which is local and much resembles that practised in rabies, viz., the immediate destruction of the bacilli at the seat of invasion by laying open the tissues of the whole complicated districts and applying chemical germicide caustics—pure carbolic acid. Ferrum candens and the fuming acids have not so much value. When treated at once (it must be remembered the diagnosis can be made with the microscope as soon as an initial lesion is noticeable in cutaneous invasion) a fatal termination need scarcely be looked for. This result bears direct relation to the timeliness and thoroughness with which the local lesion is treated. In pulmonary and intestinal infection the prognosis is as bad as it possibly can be. Recoveries have been seldom observed.

Prophylaxis.

Up to this time anthrax has been a bourne from which but few travellers have returned. As has been previously intimated, unlike the method of stamping out successfully practised in a "contagious" or obligatory-parasitic disease, it avails but little in lessening the continued dangers from anthrax to destroy the diseased animal alone, and yet that should be done with the utmost care and painful attention to detail. The farmer who has a case of anthrax on his place, the veterinarian or physician who has one in charge, even if it be in a human patient, must bear in mind that each such case is, living or dead, a veritable mortar loaded with millions of microscopic bombs, a thousand times more dangerous than if made of dynamite, which may explode and distribute a self-multiplying and almost non-destructible posterity in any locality they may fall. It must not be forgotten that the diseased or dead individual is not necessarily dangerous in the sense of a variola, a glanders, or a pleuropneumonic patient. It is dangerous from the seeds it may sow, every drop of blood, every particle of secretion, every discharge from the living, or anything pass-

ing from the dead is freighted with possible danger to the undiseased if it by any means gains access to the soil. It is a completely demonstrated fact that foulness and cadaveric changes are non-conformable to the life of bacillus anthrax in the dead, and that cadavers buried at once without any interference are absolutely without danger in time, so far as the internal parts go, there being no anthrax germs there, either as bacilli or spores. It is the discharges which may come from the nose, bladder, udder, or rectum, and be spread on the ground or stable floor, straw or bedding, in which spore development momentarily may and generally does take place, which may form permanent sources of danger to those coming in contact with them, or may lead to the development of secondary places of danger to the living. As an autopsy is absolutely unnecessary to the diagnosis of anthrax (any of the discharges, but particularly the blood and fæces answering for that purpose invariably when the animal is dead or approaching death, by the aid of the microscope), the law should absolutely forbid any autopsy or cutting up of a dead individual, or any bloody operation on domestic animals, when the disease is such as to justify even a suspicion of anthrax, except in experiment stations and places especially fitted for taking care of such cases.

Human cadavers should be cremated, as should be the bodies of all dead of dangerous infectious diseases. Animals should be burned also, were it not that it is not always so practicable as burial. There is too much danger of doing it incompletely. The greatest danger in anthrax in animals is from the manure of the diseased and in blood and secretions escaping from the cadaver in moving it and getting it on the ground. The carcasses, therefore, must be handled with the utmost care. The nostrils, rectum, and sheath, or vagina, should be plugged with old cloths soaked in strong carbolic acid, the mouth should be bound up with the same, and the carcass should be carefully watched while being moved. The hole should not be less than six feet deep for large animals and four for small ones (sheep), and large enough so that the carcass can be dumped in easily. In digging the hole the earth should be removed for one foot in depth over a space four feet wider than the proposed excavation, leaving one side free from piled-up earth to drive into. A dray, or "stone boat" is far preferable to a wagon to move cadavers. The cadaver should be dumped into the hole, if possible, without unloading. If practicable, a good covering of unslacked lime should precede the filling the hole, the last dirt being that at first dug up. In point of fact such a place should be tightly fenced in, paved, and left undisturbed for at least one year. High, dry land must be invariably selected for such burial.

In case of anthrax being diagnosed in an animal, the remaining

animals should be removed if it is possible, leaving the sick one where found infected, after their temperature has been taken. All cattle or sheep with a temperature over 102.5° F. and horses with one over 100° F. should be looked upon with suspicion in case anthrax has been diagnosed in a companion. In case the animals are pastured, the fields should be gone over carefully and, as is generally the case at the anthrax season, every especially green place, every place with stagnant water, or where the drainage is poor and land moist, should be looked on with suspicion. In known anthrax sections it should be a law that all such places should be either drained or filled, or securely fenced off. Drainage, refilling, and bringing the moisture down to that of the adjoining lands will put an end to anthrax in one or two seasons. Every mound looking as if it may have been the burial place of an animal must be looked on with suspicion, more especially if covered with a green, rich verdure, in comparison with the surroundings. If the animals are in a stable, there is not much danger to the others, provided the flies are kept out and the manure and urine can be totally disinfected. The sick animal should be killed as soon as possible after the diagnosis has been made. Not even a hair or a shoe should be plucked or taken off in remembrance; not a ball from a horn or a tag from an ear. The place where the animal has stood should be first scalded with an abundance of boiling water, to which one per cent. of corrosive sublimate has been added or ten per cent. of carbolic acid. This should be done before any litter or manure has been removed; or if removed, it should be first mixed with fine, dry, unslacked lime which should then be slacked, when the stuff can be carefully removed in barrels and then burned. After cleaning with hot water, prepared as above described, and allowed to dry, the place, floor, manger, and all should receive two good coatings of freshly made whitewash.

In regard to the human patient, the attending physician cannot be too guarded in his operations nor too careful in instructing attendants as to the destruction of wound-dressings and care in dressing the wound. No one should attend an anthrax patient, or touch a thing coming from such, or take part in disinfection if he has a wound or abrasion in the hands or exposed parts, and all should be warned against rubbing or scratching themselves with hands that have just been used about such a patient or his belongings. It is a serious question if the urine and rectal discharges of anthrax patients should not be so treated as surely to destroy the germs, even if they are to be emptied into sewers. In country districts, where they are liable to be dumped anywhere, or spread on the ground at any time, this certainly should be done. As in animals so in man, flies and mosquitoes should be

peremptorily barred admittance where the diseased are. No visitors should be allowed. Patients should be warned against the dangers of scratching themselves. The law should demand that all rags, curled hair, and wool imported from suspected districts should be first steamed in some way so as securely to kill all germs ere the employees are permitted to handle them. Employees should be cautioned against working with exposed wounds on their hands. Those engaged in working dusty material should wear some kind of dust protectors.

Regarding infection from the milk or flesh of anthrax-diseased animals it does not seem necessary to say anything in this country.

Some attempts have been made in the direction of preventive inoculation, but without there being anything definitely known as to there being any such thing as acquired immunity in the few cases that recover. "Mild cases" of anthrax seem to be unknown in animals. In man, cases of secondary infection have been reported sufficiently often to justify the assertion that "a single attack gives no protection against a second." Unfortunately in animals so few have recovered as not to give opportunity for the recording of such an observation. Preventive inoculation seems an unjustifiable attempt in anthrax; that is, it is impossible. In man something may yet be done with a bacterial germicide or antitoxin, but the way to prevent anthrax is to drain and fill dangerous lands, or where that is impossible, permanently fence them off, except for swine pastures, and to disinfect all articles of commerce experience has shown liable to be dangerous, immediately on their importation and before operatives have opportunity to come in contact with them.

FOOT-AND-MOUTH DISEASE.

BY

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BERLIN.

FOOT-AND-MOUTH DISEASE.

By the term foot-and-mouth disease is understood an acute infectious malady of cattle, which is associated with fever and the formation of vesicles. In rare cases the disease is observed also in horses, dogs, cats, poultry, and game, and it may be transmitted to man.

The localization of the disease is not always the same in animals. Thus the mouth alone is affected in horses, and is also mainly and primarily involved in cattle, poultry, dogs, and cats; the feet are chiefly attacked in swine, sheep, and goats; but in swine involvement of the snout as well is not rare. The next most common locations are the udder and teats.

The symptoms in animals consist in fever and the eruption of a vesicular exanthem upon the lips, gums, and tongue, the vesicles being filled with fluid which is at first clear and later becomes turbid. The blebs may rupture and coalesce and thus give rise to more or less extensive excoriations. Soon afterwards similar vesicles appear also on the feet, where they reach a larger size, especially under the influence of external uncleanliness, and may become very painful. Finally, in cows, the udder and teats are likewise involved. As a result of all these symptoms the animals lose their appetite and the milk becomes scanty, sometimes thick, yellowish, slimy, salty, and resembles colostrum. Besides, the milk coagulates more readily than usual and is more or less unfit for the manufacture of butter and cheese. As a rule, particularly under favorable hygienic conditions, recovery ensues in about two weeks. More rarely complications develop (inflammations of the digestive organs, myocarditis, pyæmia, hepatitis, and splenitis) and the disease ends fatally.

The extent of the ravages caused by foot-and-mouth disease among domestic animals may be gathered from the following statistics taken from a paper by Wehmer[1]: There were attacked in Germany in 1888, 82,834; in 1889, 555,184; in 1890, 816,911; in 1891, 821,130; in 1892, 4,153,539; in 1893, 500,342 animals. From among other countries we may mention that in Austria, in 1889, 506,150 animals were reported attacked, and in 1890, 156,320; in Belgium, in 1888, 230, in 1889, 899, and in 1890, 4,708. In France the scourge

appeared in 1888 in 427 localities, in 1889 in 234, and in 1890 in 79; in Italy, in 1888 in 75, in 1889 in 48, and in 1890 in 265; in Switzerland, in 1888 in 152, in 1890 in 594; in Roumania, in 1889 in 455, and in 1890 in 120 communities. In Hungary the official reports state that in the years 1889–92, 1,132,775 horned cattle, 494,533 sheep, and 434,977 swine suffered from the disease, and the loss caused thereby during 1889–90 is approximately estimated by J. Hutyra[2] at 24,000,000 kronen. According to Schneidemühl [3] the damage resulting from foot-and-mouth disease to animals attacked and killed during the years 1889–93 is fully 100,000,000 marks ($25,000,000). In England the loss caused by the epidemic of 1883 was estimated at £1,000,000 sterling ($5,000,000); in France during 1871, according to Bouley, at 30–35,000,000 francs ($6,000,000 to $7,000,000); in Switzerland the annual loss is 10,000,000 francs ($2,000,000).

The transmission of foot-and-mouth disease to man must be considered to be relatively rare, as compared with the extensive epidemics in animals. On the other hand, it is only in recent years that attention has been again directed to the disease in man, and its occurrence has been established by numerous incontestable observations.

History of the Disease in Man.

The opinion, that the disease may be transmitted from animals to man by the ingestion of milk and perhaps also by the contact of cutaneous wounds with oral and other secretions, has been expressed since the affection was first recognized towards the end of the seventeenth century. Of course the exact mode of infection was obscure, owing to the imperfect notions of the nature of the infectious agent, which was thought to be a miasm derived from the air or the ground. The first attempts at elucidating the mode of infection date from the year 1834, when Hertwig[4] and two of his assistants drank a considerable quantity of milk from a cow affected with foot-and-mouth disease, and all three in consequence suffered from the malady in a typical form. Cutaneous inoculations were also repeatedly made. Thus Bossi [5] mentions an accidental inoculation of several children with the contents of mammary vesicles from animals suffering from foot-and-mouth disease which had been mistaken for cowpox. Infection did not occur. Equally negative were the attempts at autoinoculation made by Siegel [6] with the contents of the vesicles of animals and with oral mucus.

In 1893 Schautyr[7] succeeded in producing infection of healthy cattle from men affected with foot-and-mouth disease.

As the more recent bacteriological, orrhotherapeutic, and diagnostic methods came into vogue, renewed attention began to be devoted, especially in Germany, to the question concerning the etiology of foot-and-mouth disease in animals as well as in man. Considerable stimulus was given to the inquiry by the increasing spread and rising mortality of the scourge complained of by stockmen, so that the Prussian minister of agriculture in 1893 offered a prize for the best treatise, and renewed the offer in 1895, when the amount of the prize was raised to 36,000 marks.

In the mean time the knowledge of the symptomatology of the disease had been enlarged, particularly by the communications published by Siegel,[8] Bussenius,[9] Boas,[10] G. Lewin,[11] Lindner,[12] Köbner,[13] Ebstein,[14] Glaister,[15] Stierlin,[16] and others.

A decided step toward attacking the disease in animals and hence also in man was taken by the Prussian government in 1897 by the appointment of a scientific commission, headed by Löffler, the well-known discoverer of the diphtheria bacillus, to investigate the subject. At the present time some very important results of these careful investigations are already at hand.

Etiology and Pathogenesis.

There can be no question that foot-and-mouth disease in animals and men constitutes an infectious malady, in view of its course and the mode of its transmission. Neither is there any doubt that the infectious material is to be sought in the liquid contents of the vesicles, in the secretion of the ulcers, and in the milk which has come in contact with it, perhaps also in the urine and fæces; while infection by way of the blood, by the expired air, and by the bodily exhalations is thus far not proven.

No matter whether the morbific agent is fixed or volatile, the observations of veterinarians seem to indicate that it possesses but slight resistance. Wherever a fresh outbreak has appeared many months after the extinction of an epidemic the possibility of a direct infection by other animals suffering from the disease cannot be excluded. On the other hand, a few veterinarians assert that the infectious material may remain capable of development for a considerable time in the intestinal canal of an animal as well as in the alvine evacuations.

Infection may obviously take place in either of two ways. The first is by contact; the contents of the vesicles or the secretions of the ulcers may penetrate the human skin through abrasions or lacerations. This is the reason that stable attendants are most liable to be affected

with foot-and-mouth disease. Still it is remarkable that observations of this form of infection are particularly scanty. The most natural explanation of this fact is that medical observation in the country is usually insufficient, and, moreover, that serious disease or even fatal cases are rare in man. Perhaps a single attack of the disease confers a relative or absolute immunity, thus greatly reducing the morbidity statistics, especially on account of the stationary character of the rural population.

The second and practically the most important source of infection lies in the milk and other dairy products, particularly butter and cheese. The consumption of raw milk has a special pathogenic importance, as numerous observations in recent years have shown. It is questionable, however, whether the infectious material is contained in the milk as such or only in that which has been contaminated with the contents of the vesicles. Nocard [10] has shown by experiments that milk drawn with extreme care and not tainted with fluid from the vesicles may be drank without harm. Still even under the greatest precautions the possibility of infection can hardly be positively prevented. It is still an open question whether the milk is a carrier of infection during the stage of incubation of the disease on the one hand and during the stage of defervescence on the other. As far as I know, no investigations of this point have been reported. But the milk of animals in which the process is localized exclusively on the feet must be looked upon as harmless, at least in the present stage of the inquiry. Repeated thorough boiling of the milk (not so-called pasteurization) kills the virus and renders the milk wholesome. On the other hand, as has been stated above, the danger from the milk *per se* is of minor importance.

Of more serious import than the consumption of milk is that of other dairy products—butter, cheese, buttermilk, and cream. Especially those named first, which are eaten raw, must be looked upon as most likely to spread the disease. This statement is borne out by a number of reported cases in which the infection could be traced with the greatest probability to the consumption of butter or cheese (Ebstein,[11] Case I.).

As regards the spread of the disease from man to man and its mode of propagation, sufficient observations are not as yet available. In the epidemic of the year 1891 in a village not far from Berlin, described by Siegel, the spread was exceedingly rapid. As a rule several members of a family were attacked in quick succession, and soon after the inhabitants of adjacent houses. Of interest in this connection is also an observation by Lindner,[12] which was most probably an instance of foot-and-mouth disease. At the surgical clinic

a child known to have drank raw milk was first taken sick, then followed the child in the next bed, then the third lying beside the second, and so on through the whole of one side of the ward, the opposite side remaining free. As every child used its own eating utensils, infection by this means seemed to be excluded. Direct contact of the children was also out of the question, as all of them had been operated upon and were confined to the bed.

However, this instance proves nothing against local infection, and obviously cannot be pleaded for the theory of air infection. It is precisely the fact that always the children lying in adjoining beds suffered and not those on the opposite side which speaks against this hypothesis.

Pathological Anatomy.

The few published pathologico-anatomical reports give us but an imperfect picture of the changes in the organism caused by the disease, at least in man. At the autopsy of a child Demme found the liver friable, symptoms of acute swelling in the spleen and kidneys, acute catarrh of the mucosa of the small intestine, and occasional ruptured lymph follicles, without perceptible ulceration. In the case of a two-year-old child mentioned by Siegel [8] there was swelling of the solitary follicles of the colon with superficial ulcerations at their tips. Similarly, Peyer's patches and the mesenteric glands were also reddened and swollen. The spleen was not enlarged, its color was partly normal, partly light yellowish-red, and no follicles were visible. The liver was soft, large, and appeared marbled on section. A few glandular acini were light yellow and surrounded by a dark-red areola. No changes could be observed in the kidneys. At the external genitals considerable swelling was noted in the skin, which was discolored to a dark reddish-brown; on the lips, the upper one in particular, were ulcerations covered with a hemorrhagic coating. Several hemorrhages were visible on the skin of the abdomen.

In a case of infectious glossitis, coming from a locality in which numerous instances of epidemic foot-and-mouth disease had occurred, which was observed by E. Rose,[19] of Berlin, the autopsy disclosed the following alterations: Œdema of the pia and of the cerebral substance, slight leptomeningitis, pulmonary œdema in both upper lobes, and adjoining the root of the right lung a softened area the size of an apple. The spleen was not increased in size, but the liver was enlarged and soft (fatty liver). Here and there were yellowish-white areas, ranging in size from that of a pin's head to that of a pea, which on microscopical examination proved to be agglomerations of fat globules. Both kidneys were in a state of inflammatory swelling.

The tongue was thickly coated, enlarged, but free from abscesses. In smear preparations from the liver and kidneys Siegel was able to demonstrate bacteria which he held to be characteristic (see below).

Bacteriology.

The first statements as to the presence of microbes as the cause of the foot-and-mouth disease are to be found in the seventh decade of this century. Hadinger, Flemming, Spinola, and Zürn found forms resembling oidium albicans in the ulcers due to the disease. Bollinger[20] first demonstrated in the fibrinopurulent coating of the oral ulcers numerous microorganisms, small bacteria and cocci, which were situated between the pavement epithelia. Kitt[21] discovered micrococci both in the contents of the vesicles and in sections, but was unable to prove any connection between the organisms and the disease. Nosotte[22] found in the clear contents of the intact vesicles a motile micrococcus which when transferred to other animals produced the disease as did the serum. Libbert[23] cultivated a microorganism from the contents of the vesicles and from the milk of affected animals at the height of the disease, but the organism failed to prove pathogenic when inoculated upon healthy animals. Klein[24] found in the contents of the vesicles and in the tissue of the pustules of sheep, streptococci, cultures of which, when fed other to sheep, produced typical foot-and-mouth disease, and the same organisms were present in the vesicles.

Siegel[8] cultivated from the liver and the kidneys of human and animal cadavers a bacterium resembling the colon bacillus. This microbe was 0.5 μ long and oval in shape; its colonies on gelatin developed fine radiations. Pure cultures were inoculated upon a pig and two calves; vesicles which subsequently turned into ulcers developed in the mouths of all the animals and in the latter also in the nose. Bussenius[9] cultivated from the contents of the vesicles, from the secretion of the ulcers, and from the saliva of a patient an ovoid bacillus closely resembling that of Siegel. Pure cultures inoculated upon calves and a pig produced changes which rendered the existence of foot-and-mouth disease most probable.

Behla[25] and Schottelius[26] cultivated protozoa, the former from the contents of the vesicles and from the blood. In the hanging drop the organisms presented a varying size, changes in shape, and spontaneous movements. The same forms could be found also in the saliva, in the spleen, and in the epithelium scraped from the mucuous membrane. Quite recently Behla has also reported the successful transmission of the disease by friction with fresh infectious material.

From the contents of the vesicles Schottelius cultivated forms like a string of pearls; they bore some resemblance to certain amœbæ. He called them "streptocytes." They stain with gentian violet and according to Gram's method, but they react with difficulty to methylene blue. They grow only at a temperature of 37°–39° C., best in agar-gelatin containing glycerin or formate of sodium, or in bouillon having a similar composition. An experimental inoculation proved negative.

Kurth[27] described several streptococci, one of which, owing to its constant presence, was looked upon as the probable cause of the disease. Inoculation experiments failed.

Finally Starcovici[28] also found a bacillus which moreover was said to diminish to less than half its size in passing through the animal body[?]. This author likewise succeeded in transmitting the disease by cultures of his bacillus.

The question has assumed quite a new phase through the labors of the commission appointed to investigate foot-and-mouth disease, whose report has recently been published by Löffler and Frosch.[11] They found in the first place that no bacteria of any kind occur in the contents of the vesicles, and that the lymph, of course taken with all due precautions, remains free from all bacterial growth after several weeks' observation and upon the most variously constituted media. Nevertheless the lymph proved to be unquestionably the exciting cause of the disease, for calves and heifers inoculated with this material always suffered from the disease in its typical form after from two to three days. The above-named investigators therefore consider all the reported findings of bacteria as accidental. Special examinations with reference to the inoculations by Siegel and Bussenius showed that inoculations and pure cultures of the ovoid bacillus may indeed produce serious disease in calves, but not the typical picture of foot-and-mouth disease. The effect of the virus was equally pronounced whether the lymph was used in its natural state or after it had been filtered through silicious earth and thus rendered free from bacteria in the ordinary acceptation. Indeed subsequent calculations showed the virulence to be equal to 1:7,500,000,000 of pig's blood, hence to exceed by far the virulence of all known toxins. Löffler and Frosch therefore believe that such activity can be produced only by small living organisms, whose size, however, must be beyond the limits hitherto attainable by the best microscopes. The same view would perhaps also explain the negative bacteriological results thus far obtained in smallpox, scarlatina, measles, typhus fever, cattle plague, and other diseases. The same investigators also reported some successful attempts at immunization which will be discussed in the section on prophylaxis.

Clinical Course.

Foot-and-mouth disease in man occurs either sporadically or epidemically. The epidemic form is always exceptional; as in the epidemic described by Siegel, it seems to be favored by bad hygienic conditions, defective sewerage, unhealthy habitations, and lack of cleanliness.

According to the material thus far available, including that of the last few years, the clinical course shows great differences, so that a generally satisfactory description presents some difficulties. Some cases described as foot-and-mouth disease will not bear strict criticism. Even the character of the epidemic reported by Siegel as foot-and-mouth disease is doubted by a few observers such as Ebstein, Hutyra, and others. It may be admitted that Siegel's material, being composed exclusively of ambulant patients from the lowest classes of the population, is naturally lacking in reliability. Still it would be going too far if we should question the nature of Siegel's epidemic solely because all the symptoms do not tally with the picture of the disease known up to that time. Even now it may be stated as a fact that a variation in the virus causes different degrees of intensity in the symptom complex; that there are on the one hand abortive cases with slight if any subjective manifestations, and on the other hand instances of serious disease occasionally associated with grave anatomical alterations and even fatal termination. Children in particular seem powerless against the virus; at least in Siegel's epidemic a considerable percentage of the fatal cases occurred in children during the first years of life.

The duration of the *period of incubation* varies between two and ten days, according to the published statements. In favor of a short incubation are the animal experiments and some positive infections in man. Thus Esser reports the case of a veterinarian who had infected himself with a handkerchief that he had used during the examination of cattle. The following day he suffered violent pain in the head and limbs; the second day fever set in, with a sensation of formication in the hands and feet; on the third day, while the fever declined, an aphthous eruption appeared in the mouth, on the tongue, the lips, and the side of the nose.

The disease itself always begins with fever of varying intensity (38°–38.5° C.=100.4°–101.3° F., in children occasionally 39°–39.5° C.=102.2°–103.1° F.). At the same time the patients experience great debility, pains in the limbs, malaise, and attacks of vertigo which may be intensified to epileptiform conditions. After this pro-

dromal stage has run its course, a peculiar eruption develops partly on the lips and especially on the mucous membrane of the cheeks, mouth, and tongue, as well as in the region of the nose. The eruption is vesicular in character, and the individual lesions may reach the size of a pea and subsequently become larger by confluence. The vesicles contain at first a clear watery serum which later becomes turbid. When the blebs rupture crusts form on the lips and in the region of the nose, and excoriations on the oral and buccal mucous membrane. In some cases there is at the same time marked swelling of the lips, the alæ nasi, the eyelids, and particularly the tongue, which may occasionally project from the mouth and if the œdema increases may even become partly necrotic, as in a case observed by Siegel. This local affection of the mouth may be associated with vesicles over the whole body or over parts of it. "These vesicles and bullæ, at first merely the size of a millet seed and filled with clear contents, enlarge rapidly, the fluid soon becomes purulent and turbid white, and they present the appearance of medium-sized ordinary pustules. They are usually discrete, but they also coalesce, especially around the nails and on the dorsal surface of the phalanges. Recovery as a rule takes place in two or three weeks without injury to the nails. Only in rare cases a severe onychia develops with mortification and shedding of the nail" (Bollinger).

The local affection of the mouth naturally causes a number of serious symptoms, consisting partly in pain, interference with speech and deglutition, partly also, especially when the tongue and nasal mucosa are implicated, in impeded respiration. Reflex excessive secretion of saliva and mucus, sometimes mixed with blood, has been often observed.

The temperature usually falls with the development of the vesicular eruption. The latter in uncomplicated cases persists about two to four days, when drying and crusting set in, to be followed as a rule by complete recovery, with restored appetite and subjective well-being. The entire duration of the disease in the slighter cases is about eight days; in the more serious cases from four to eight weeks may elapse before recovery is complete.

The typical morbid picture may be modified by complications which may transform the disease into a grave disorder and endanger life. Among such complications are the intestinal symptoms (exhausting diarrhœas), hemorrhages from the oral mucous membrane, and more or less copious intestinal and renal hemorrhages. Thus the morbid picture may present the closest resemblance to scurvy. On the other hand, affections of the respiratory tract—bronchitis and catarrhal pneumonia—have also been observed. Finally the

nervous system may likewise show considerable disturbances, as manifested by spasms and paralyses.

According to Siegel, besides the acute form of foot-and-mouth disease a chronic form also occurs, which is symptomatically but imperfectly characterized, and manifests itself rather by general disturbances, such as vertigo, loss of appetite, constipation, and great prostration.

The *termination* of the disease in sporadic cases seems to be without exception favorable. Only in its epidemic spread we meet, along with the lighter, also some grave cases which result fatally by complications, hemorrhages, exhausting diarrhœas, etc. Children, old people, and persons whose resisting powers have been weakened by preceding disease are particularly liable to succumb.

In a few epidemics the mortality was considerable. In one epidemic observed by Hulin[36] twenty-three in every thousand inhabitants perished. In the epidemic observed by Siegel, thirty-six persons died in the course of two and a half years, and in another epidemic fourteen.

Diagnosis.

The diagnosis of foot-and-mouth disease presents no difficulties when direct transmission from animals to man can be clearly demonstrated. Thus it can usually be easily made in milkers and stable attendants in general. The question is far more difficult, however, when the intermediate links between the infection and the disease in man are lacking. The proved ingestion of raw milk or of cheese and similar products does not always justify the diagnosis of foot-and-mouth disease, even when such articles of food come from an infected region; for it has been stated above that the milk, unless contaminated with the products of the virus, is not an invariable carrier of the infection. Therefore, though the objective symptoms point to an epizootic, the diagnosis can be stated as merely a probable one. Obviously the weak point in the epidemic observed by Siegel lies in the difficult demonstration of the connection between the source of infection and the disease in man. However, as the period of incubation ranges between two and at most ten days, there is a possibility in some cases of proving the existence of an epizootic.

The only way of making the diagnosis positive is, as Schneidemühl[3] proposes, to inoculate small animals, such as goats and sheep, with the lymph from the vesicles. This suggestion, however, is to be recommended only in the case of larger epidemics of doubtful character.

The differential diagnosis may present great difficulties, as is shown by observations recorded by Siegel and Ebstein.

The differentiation from simple aphthæ is easy, as the latter disease never runs its course with violent prodromes, vesiculation, serious ulcerations, and intestinal symptoms.

Ulcerative stomatitis always presents a necrotic character and besides remains local. General symptoms are never noted in the adult; they may occur, however, in children and give rise to mistakes. Vesiculation and cutaneous exanthems do not come under observation in ulcerative stomatitis.

Other diseases coming in question are scurvy, occasionally also measles, typhoid fever, and septicæmic conditions. A differentiation will always be possible, however, at least after prolonged observation.

In a case cited by Lewin[11] the differential diagnosis finally lay between syphilis and foot-and-mouth disease. The case was that of a farmer suffering from an ulcer on the penis. Examination revealed small vesicles on the prepuce and in the retroglandular sulcus. The diagnosis of foot-and-mouth disease was established by the fact that the patient had similar vesicles on one hand and on the lower lip. He came from a region in which foot-and-mouth disease prevailed.

Prophylaxis.

As in the case of all infectious diseases, the prophylaxis is of paramount importance in the fight against the malady. Leaving aside the prophylaxis of the disease in animals, which naturally includes the prevention of the transmission to man, and restricting ourselves in the main to the prophylactic measures regarding the malady in the human subject, the following points come under consideration: First and foremost, the direct transmission by contact of the affection from the lower animals to man must be guarded against. As this point depends, aside from a few cases of accidental infection, upon contact of the country people, especially milkmen and maids, with the diseased cattle, prophylactic hygiene must aim to point out the danger of infection, and particularly to take care that such dairymen and women as suffer from erosions upon the hands, feet, and face be kept from milking, if at all possible. This remark applies above all to children, to whom in some country districts the act of milking is left by preference, all the more because, as stated before, children are predisposed to grave forms of the disease. As it is still an open question whether men acquire immunity by an attack, and as the report of Siegel's epidemic seems to indicate even that repeated attacks occurred in the same individuals, the same precautions should be taken,

until this question is decided, with persons who have before suffered from the disease.

The sick must be isolated as far as possible from other persons, though this rule will probably be difficult of enforcement, owing to the close quarters and the slight regard for hygiene among the country people. It will probably be best to direct such patients at once to the nearest district hospital provided with isolating facilities, where they should remain until completely recovered. Little is to be expected, however, from disinfection of the rooms which the patients have occupied, for experience teaches that this is hardly feasible in the country, and besides no effective and at the same time innocuous method of disinfection is thus far known. It will be well, therefore, to restrict ourselves to the removal of the eating and drinking utensils which have been used by the patient whenever they cannot be sterilized by boiling.

The second prophylactic measure applies to the dairy products obtained from diseased animals and the consumption of the flesh of those affected with foot-and-mouth disease or which have died of it.

The questions involved in this part of the subject have been largely discussed of late by hygienists, physicians, veterinarians, and farmers, but without any agreement as to rules and methods for an effective prophylaxis.

The nearest approach to unanimity is with reference to the milk. As this can be made absolutely germ-free by sterilization there is no difficulty in its sale. But unfortunately for the dairyman, the milk of animals affected with the disease becomes more or less unpalatable, so that the public is apt to be suspicious about such milk, even when it has been freed from germs by boiling, and often refuse to buy it even when it is sold at a lower price. The best plan seems to be to mix such milk after careful sterilization with healthy milk, thus producing at all events a more palatable preparation.

Much greater difficulty is presented by other milk products—butter and cheese—the preparation of which, as is well known, begins with fresh milk spontaneously fermented. It must remain a matter for future consideration what steps should be taken to protect the farming interests without at the same time violating hygienic rules, and exposing the consumer of these milk products to the very real danger of contracting foot-and-mouth disease.

Similarly, great differences of opinion still prevail as to the use of the flesh and edible organs of animals affected with the disease. The most radical proposition is to destroy such meat and organs outright. For the present, it is probable that the authorities will have to be satisfied to allow the flesh of slightly affected animals to be sold after

removal of the diseased portions; in grave cases, especially those in which the stomach and bowels are involved, the use of the flesh should be allowed only after it has been thoroughly cooked. At all events, during the prevalence of an epidemic of foot-and-mouth disease at least, the public should be advised to avoid raw meat on principle. A proposition which appears of doubtful propriety has been made by Ostertag,[31] namely, to allow the flesh, especially the valuable tongue, to be sold after scalding; obviously in this way the noxious material will be but imperfectly destroyed.

It would be of the utmost importance as regards the prophylaxis of the disease, especially in man, if it were possible to cure or at least to mitigate the affection by immunization. The most recent results obtained by Löffler and Frosch[11] offer very fair prospects in this direction. At the time of the present writing investigations are being made on a large scale, and with every precaution, with reference to immunization. It is still too early to express an opinion as to whether immunization of man is likewise possible or whether it will be at all necessary if the animal experiments in this direction should be successful.

Treatment.

The treatment of foot-and-mouth disease is to be directed chiefly against the inflammatory and ulcerative processes on the mucous membrane of the lips, mouth, tongue, and pharynx. A number of the ordinary remedies used in such cases have been recommended for this purpose. Among these are potassium chlorate as a gargle in two to five per cent. solution, and borax (five to ten per cent.). Siegel,[8] who probably was in position to gather the most extensive therapeutic experience, recommended brushing with silver nitrate solution (0.3–1 part in 15), repeated several times a day. Ebstein[14] in one case had a very favorable result as regards both the pain and the healing of the ulcers from a one-per-cent. spray of boric acid.

Of internal remedies Siegel recommends preeminently sodium salicylate in doses of 8 to 10 gm. daily.

Otherwise the treatment will be expectant and dietetic. When complications occur, such as diarrhœa, hemorrhages, and cardiac weakness, they will require appropriate treatment, which need not be discussed in this place. The cutaneous exanthems may be dusted with suitable powders, such as dermol, airol, alumnol, etc., or zinc or salicylic pastes may be applied. The diseased parts may also be treated with antiseptic lotions containing lysol, solveol, or potassium permanganate.

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ACTINOMYCOSIS.

BY

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ACTINOMYCOSIS.

It is only about twenty years since actinomycosis was first recognized as a distinct and independent disease, and yet among the many diseases which within that period have been discovered and described, there is hardly one which is so quickly recognized or one which so soon convinces us of the relation between cause and effect. The reason for this fact lies certainly, at least in part, in the unmistakable appearance of the parasite, sometimes visible to the naked eye, through the action of which upon the human or animal body a distinct but exceedingly polymorphous disease of a more or less chronic nature is caused.

History.

The first investigation in which cattle were the subject we owe to Bollinger. In 1876 he described in these animals an affection of the inferior maxillary region which in its external appearance showed only slight analogy with human actinomycosis. From the etiological similarity, we are compelled to identify as the same disease what we see in man and in cattle, just as tuberculosis of cattle which appears at first glance to be different from the disease in man must be identical with it because it comes from the same infecting cause.

The sulphur-colored granules to which Bollinger attributed such an important rôle in the process had already been observed, for Rivolta, Perroncito, and others had demonstrated them as early as 1845, thus long before the discovery of actinomycosis bovis; and von Langenbeck had shown, in a pus sac situated in front of the spinal column, the presence of the characteristic yellow granules whose parasitic nature he suspected. Still all these authors had not recognized any causative significance in these granules, but had only considered it as an open question whether such granules were of a vegetable nature, *i.e.*, fungi. Bollinger, on the other hand, did not demonstrate anatomically what Hars designated ray fungus (*Strahlenpilze*), from the concentrically radiating structure of the gland-like colonies, and which he found without exception in the swellings of the jaw, tongue, and neck in cattle. He nevertheless described the qualities of that substance, resembling sometimes granulation tissue,

sometimes a new growth, which permeates the tissues in this disease. Independently of these results of Bollinger, Israel observed the occurrence of the same parasite in man, but, apart from this outward resemblance, the disease did not betray the least similarity with the symptom complex described by Bollinger. In 1878 this investigator published a treatise[1] which demonstrated a clinical picture specially characterized by the presence of the fungus, but not otherwise well marked, so that at the time he considered it as a kind of chronic pyæmia. It was reserved for the present writer[2] to designate as "actinomycosis" a peculiar case of prevertebral phlegmon which he met with in 1879, and in which he found the well-known granules familiar to him from his experience with cattle as the ray fungus; and through this and other observations he thus introduced the subject of actinomycosis hominis.

ACTINOMYCOSIS IN CATTLE.

The disease in cattle manifests itself in a well-marked swelling of the lower portion of the face, and a spindle-shaped enlargement of the lower jaw and region around it. The tongue is not infrequently involved. This swelling depends upon the development of a peculiar fleshy growth, sometimes of a gelatinous, sometimes of a fatty nature, in the substance of the under jaw. The process extends from the interior outwards towards the *corticalis*, which is eroded in many places or completely perforated. The periosteum then becomes changed by a process of dense thickening with fistulæ perforating it in many places and extending into the soft parts, which later are themselves gradually destroyed here and there. We also notice in the case of such animals a general fleshy swelling sometimes with a series of fistulous openings out of which there is a discharge of a serous or purulent fluid. The discharge differs from other wound products in that it is characterized by the presence of the peculiar yellow granules sometimes visible to the naked eye, which are called the ray fungi and which are the cause of the disease. If we cut or saw through such a jaw, we find its cavity and most of the *corticalis* changed into a firm fatty mass by which the alveolar nerve and accompanying blood-vessels are completely surrounded and covered. In addition to this firm ground substance, we notice not infrequently smaller or larger cavities, filled with greenish pus and a relatively large number of those ray-fungus granules. Neighboring portions where the fleshy tissues are involved in various stages of softening, although not yet the seat of a suppurative process, are well suited to show us how these areas, apparently of such different character, really are closely related.

By more careful examination we can make out distinctly how in those apparently firm masses, irregular strands of a much softer substance run. They are the irregular canals which have numerous branched processes filled with gelatinous granulations and usually with fresh pus, or with only serous fluid containing the characteristic fungus granules. Only when they are distended do they show well-marked collections of pus surrounded by a thickened layer of moist and pale granulations covered with orange-colored spots.

An extension of the disease over the face and neck occurs among cattle only exceptionally. In any case, such a thing occurs much later than in man.

New facts as brought forward by James, Ponfick, and other authors, allow us to recognize in man, as a rule, a somewhat different clinical as well as anatomical picture, namely, the appearance of a chronic "phlegmon" in the form of a destructive inflammation, first local, then gradually spreading, with here and there a tendency to purulent degeneration. I observed in one of my earliest cases that these peculiar growths have the power, like that of the malignant tumors, of breaking into the vascular system and causing disease of the same kind in far distant organs. By this evidence, then, that actinomycosis can cause by metastasis similar growths in distant portions of the body, as is so common among cattle, it is believed that the identity of actinomycosis in man and in animals is established, for it is undeniable that not only is the same parasite responsible, but that under favorable circumstances the pathological products are similar.

It may be mentioned in this connection that this new-growth-forming tendency is only facultative in the ray fungus, and I believe that, in man, the products which are formed by this parasite in the tissues can be considered as infection-neoplasms, such as occur also in tuberculosis, leprosy, and syphilis, a view which has undeservedly excited the opposition of such a capable writer as Bostroem.[1]

Geographical Distribution.

During the past ten years many records of cases have been collected from various sources, so that the extension of the disease throughout the Old as well as the New World cannot be doubted. In addition to many confirmatory observations in Germany, there are numerous reports from Austria, Switzerland, England, and Russia, scattered instances from Denmark, Roumania, and other countries, and later from several American states and from France.

The more that experiences from foreign countries have been ana-

lyzed the more certain does it appear that actinomycosis is not native in the western hemisphere. The works of Byron,[4] of Hodenpyl,[5] of Murphy,[6] and later of Mallory[7] show this to be the case in the United States. Similarly, in South America, the contributions of Bulhões[8] are important. The disease is absent from Melbourne as MacTuerney states (1889), and Humphry Marten[9] confirms this in the case of the cattle, on the one hand, in Tasmania, and of man, on the other, in Australia.

Etiology.

Since the pathological condition has been well understood and the nature of the disease well established by an ever-increasing number of observations, the etiology of the subject has made great advances, not only by more careful examination of the exciting causes of the disease, but especially by inoculation experiments by Afanassiew,[10] Bostroem, and Max Wolff and Israel.[11] In reference to prophylaxis, the evidence secured by Johne,[12] Soltmann,[13] and others, that the spicules of certain kinds of cereals serve as carriers of the disease was of very great importance. This knowledge, important as regards the prevention of the disease, must appear all the more important since the treatment during the last twenty years has hardly been changed from its original method, namely, to remove with as much care as possible, by means of the knife and the sharp spoon, all the disease to its deepest points of invasion.

Natural History of the Ray Fungus.

The points by which the ray fungus may be distinguished from other microorganisms are, under the microscope, so distinct that its recognition by even the least experienced may be considered an easy task. The fact that the reported cases to-day are already five hundred in number is not to be explained by an increase in the disease, but by the fact that it was formerly unrecognized and was confused with other chronic infectious processes, especially tuberculosis and "scrofula," and to some extent with syphilis. None the less is it possible that many indolent phlegmons, from the slowness of their course, and certain cases of pyæmia whose origin and manner of development have been obscure, have been taken for actinomycosis.

Whether it is in the pus which flows from the fistulous openings or the cavities, or whether it is in the mass of spongy granulations, we can distinguish, even with the unaided eye, the round fungus granules which are usually embedded in a mass of pus. They are easily distinguished by their dark-yellow color from the yellowish-

white pus, and to the attentive observer they are unmistakable. Under the microscope, they appear as balls or round masses singly or in heaps. With moderate pressure upon the cover-glass, these balls spread out into a number of processes in which are at once visible the characteristic "rays." The whole affair reminds us of certain sea algæ, or of a wreath, and consists of closely packed fine threads in a radiating arrangement. The peripheral end of these threads shows a considerable swelling, club-shaped, with here and there branches or hand-shaped prolongations which include the whole surface, and the more marked they are the more completely do they cover the finely threaded centre. For the rapid identification of its presence it is a good plan to treat the suspected pus with a strong acid or a strong alkali. By this method the fungus is not injured or changed, but shows itself much more distinctly in its clearer environment.

In addition to these larger conglomerations with a distinct sulphur color, we meet with still smaller balls of a gelatinous appearance, which consist of grayish granules. These represent the earliest developmental condition, and consist substantially of a thick mass of threads. These are either entirely simple or branched, and at the centre are closely interwoven with one another. The farther from the centre, the more loosely placed are they with regard to each other. They do not, however, lose the ray-like arrangement entirely at any point.

Very often the round or elliptical masses of actinomycotic formation possess a pedicle formed from the threads which passes into the smaller ball. Bostroem has called this the root tress-work. At the periphery the threads become bulging as a rule, and end with the appearance of well-formed actinomycotic nodules. In addition we often see formations, sometimes large, sometimes small, which appear only indistinctly marked, or we may miss such structures altogether. These formations were formerly considered to be immature stages in the development of the fungus. Bostroem, from careful investigations, is, however, of the opinion that these structures are entirely products of degeneration, depending upon a gelatinous distention of the fungus threads in consequence of unfavorable conditions of growth acting in both the earlier and the later stages of development. He also considers the dichotomous or finger-like protrusions to be of the same nature, although many writers have thought them to indicate beginning or progressive sprouting, and he refers their origin to tears or ruptures of the older and more friable formations. Following this idea, he regards those granules, consisting entirely of threads, as the youngest and most active specimens. Under all circumstances this knowledge is of great practical importance, for the frequently de-

scribed branched swellings are a very common but in no way indispensable attribute of actinomycosis, since they may be absent in the youngest and to all appearances most active forms of the organism. The diagnosis, then, of actinomycosis may with entire correctness be made in their absence if the other important characteristics of the disease are present.

In order to get a clearer result the Gram method of staining is to be recommended. For the purpose of getting a differential stain, a preliminary treatment with aniline gentian and then the use of Wei-

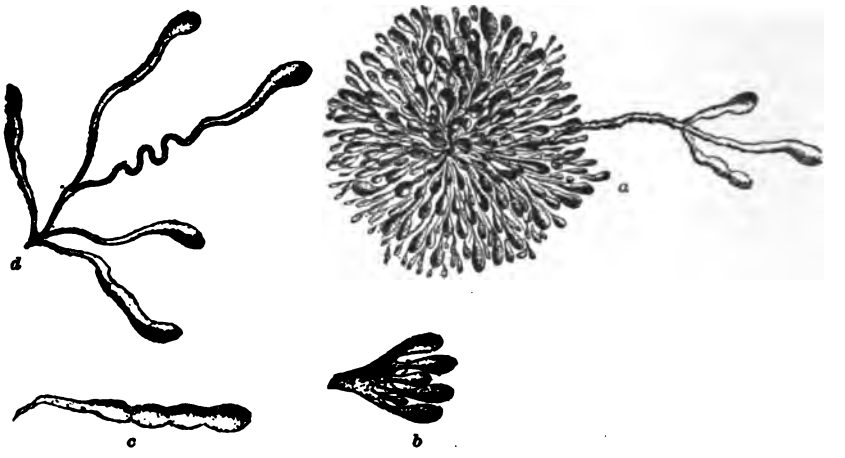

FIG. 4.—Actinomyces. *a*, Perfect form of fungus. A long filament terminating in bulbs is given off at one side; *b*, peculiar formation of bulbs; *c*, beaded form; *d*, branching of bulbs from hypha.

gert's picrocarmine are advisable. Sections may be washed in water, and then in alcohol, and may be mounted in the customary manner. The threads will then show blue, and the nodular processes red.

A mass of fine, branched threads forms the starting-point for the further development of the nodules, and the more this root mass increases at its origin the more clearly are we able to make out an inner firmer and an outer more loosely formed layer, the latter being always of clearer structure. In the course of the further development of this at first simple structure, there are formed granular groups which assume a rosette or flower-like form. Such collected forms are those in which we find each nodule well circumscribed, and in which we begin to see the formation from the same sort of threads which form the main portion.

The chief portions of the separate masses are very diverse in their constituent elements, consisting partly of collections of cocci and

partly of bacilli. The latter are sometimes single and sometimes of variable dimensions, branched and containing spores, or with club-shaped processes. On this account Bostroem thinks that the ray fungus belongs to the polymorphous bacteria.

Cultures.

The earliest successful culture experiments were made by Bostroem. He mixed fresh material from actinomycotic foci on plates with gelatin. The colonies which grew here he transferred to blood-serum plates. On these, in about twenty-four hours, best at a temperature between 33° and 37° C., colonies, looking under the microscope like dewdrops, appeared, and were whitish or yellowish in color. After fourteen days the spots became pretty distinctly actinomycosis colonies, especially in the deeper portions of the cultures. Since, according to Buchner, the anaërobic cultures have succeeded, we may classify the organism of actinomycosis as a facultative anaërobe. The observations of Bostroem that agar-gelatin cultures, even after a long time, and even if entirely dry, may still contain living organisms, is noteworthy in this connection. The young, minute yellow forms, only about twelve hours old, consist of coccus-like granules from which one or two threads extend. In the course of the first day there are visible both simple and branched threads. After thirty-six hours septa or dividing planes appear in these. Later we notice on the ends of the threads knob-like enlargements whose appearance is that of the well-known specimens seen in man. M. Wolff and J. Israel were the first to see in cultures the short comma-like forms.

Inoculation Experiments.

In order to decide upon the value of the evidence in cases of inoculation experiments, Bostroem made the attempt in vain to infect the peritoneal cavity with the products of these inoculation attempts. Wolff and Israel were successful in a series of experiments and saw tumor-like masses result, which were characteristic. These masses contained a thick felt-work of granules and likewise fork-shaped rods. From the positive results of culture experiments we may consider as proven the transmissibility of actinomycosis by inoculation.

ACTINOMYCOSIS IN MAN.

Etiology.

What first concerns us in the mode of infection in man is the condition under which the ray fungus can invade the organism. It cannot be doubted that a direct transmission from animal to man may

occur, and a large number of observations upon this point have been made among those concerned with the care of cattle and other domestic animals; and furthermore, we may consider, according to all evidence, a direct inoculation of this exogenous parasite in the human organism as common. Since Johne showed that the ray fungus not uncommonly grows upon cereals, a mass of evidence has been accumulated which confirms the occurrence of this mode of infection. Sometimes the swallowing of grain or of a piece of grain stalk acts as the cause of the disease; sometimes the penetration into the tongue or œsophagus of a spicule, when such happened to contain the organism. With reference to the frequency of that sort of occurrence, and in order to show that at least in recent cases the possibility cannot be denied, Bostroem states that he believes that the infecting power may be very great even if, as is indeed the rule in chronic cases, hardly any signs are visible in the early stages.

In this connection we may mention a very interesting observation of Birch-Hirschfeld,[1] in which the history of the case was negative, and in which there was found in the lung in the apex a cavity the size of a bean, with the tissue broken down, which contained a foreign body about 1 cm. long, and seed-like in shape, partly in the soft tissue of the cavity wall and partly in the cavity. It was a grain of barley with actinomycotic vegetations covering it. In a similar way there has been seen a vermiform appendix, filled with inspissated fecal matter, containing an incrusted piece of straw. Consequently it cannot be denied that the disease can be disseminated in other ways than the usual ones, for instance, through carious teeth and apparently also by infection from the secretion of the tonsillar crypts. Although the teeth can act as the channel of entrance of the disease by such a gross method of transmission as direct transfer of the infection, the dental surgeon will sometimes meet cases in which actinomycosis is present in the crypts of the tonsils. In any case we may in the presence of either of those two common modes of infection, as from an accident or in extracting a tooth, discover a wound through which inoculation may occur in the alveolus of a tooth, in the gums, or in the substance of the jaw, from fungi already present on the teeth. Likewise opportunity has not been lacking for seeing cases, as the writer has described, of infection from barber's utensils, and cases in which the disease began in the upper jaw after the extraction of one of the back teeth. In rare cases the carrier of infection has apparently been isinglass, and in other cases splinters of wood or often unknown substances.

Modes of Entrance and Diffusion.

With such a number of possible modes of entrance, and of canals through which the disease may be diffused, and by reason of the length of its course, it is distinctly important to distinguish the different methods of diffusion of the disease. We may conveniently consider that there are four groups or localities of distribution of the disease. But it is to be remembered that each of these four forms of the disease has one central characteristic manifestation, and may show other smaller local outbreaks at various points. The foci occurring in the neck may often be referred to infection from penetration of the fungus from the mouth, from the tonsils, or from the œsophagus. The localization at the level of the middle and lower dorsal vertebræ shows itself by an extension of the process from the lungs to the costal pleura and then into the fleshy masses of the longissimus dorsi. Involvement of the peritoneum by a perforation from without, or from the intestine, may be considered to serve as another form of regional disease. All those forms of cereals which have stiff or thorny processes or hooks may serve as carriers and propagators of the disease. These spicules fasten themselves in the tissues of the viscera and gradually bore small canals for themselves, which sooner or later reach the surface and cause fistulous openings. The canals formed in this way furnish the means for the penetration of the youngest and most vigorous fungus colonies.

Furthermore, it cannot be doubted that the propagation of the disease may be assisted by wandering fungus cells, such as might be floating in the air.

The above-described tendency of many cases of actinomycosis to the formation of extensive fistulæ, to extension with the appearance of chronic phlegmon and progressive infiltration of the subcutaneous and muscular tissues, appears in marked contrast with the very acute manner of the development of the disease in cattle.

Nevertheless, in the disease in man the tendency to the production of vegetative growths may be absent or present only in a slight degree. The tendency to new-growth formation, however, limits itself much more to the formation of fungus-like, apparently indifferent granulation tissue. It may be that this quality depends upon a less marked plastic power of the human tissue in resisting the extension of the actinomycotic disease, thus causing the formation of flabby, unhealthy-looking granulation tissue, with early fatty degeneration. This fact is of practical importance, for upon it rests our first information concerning the nature of the crange-colored tissue, which con-

sists of a thick massing of the fungus granules and their fatty detritus in addition to the gelatinous granulation tissue, by means of which we are able to distinguish cases of simple suppuration from disease of actinomycotic origin. The condition of the granulation tissue, as we have described, in such cases furnishes us with reason for careful microscopic examination of the discharge from the sinuses. In case that test confirms the presence of the characteristic fungus granules, we have reason for a certain diagnosis at once. The accuracy and trustworthiness of such a conclusion have been shown numberless times, and the confirmation of a conclusion thus formed is specially to be thought of in connection with the number of early diagnosticated cases in which a disease of obscure origin should have reached such a very extensive dissemination in so short a time.

With reference to the nature and the origin of purulent elements in the discharge, two things must be emphasized. First comes the element in the discharge, consisting entirely of pus-like matter from the sinuses and the cavities connected with them, containing blood cells and broken-down granulation tissue. It is unquestionable that the discharge not infrequently is nothing more than ordinary pus, and in such cases we may consider that we are dealing with a mixed infection caused by the entrance of various pus-producing organisms into the sinuses and their communicating canals. It is evident from this variable character and origin of such cases, and considering the clinical significance of the purulent products, that this is very important. We must remember, furthermore, that hand-in-hand with the destructive process in the tissues there are associated complicating processes caused by the bacteria of suppuration. All of the extensive spreading in such cases is in the direction of the loose cellular planes of tissue, both subcutaneous and intermuscular. The already existing natural lymph channels do not as a rule furnish means for spreading the disease, as can almost without exception be demonstrated by an examination of these vessels. Therefore the propagation of the disease through the body, as the writer has so convincingly shown, must be to a large extent through the blood-vessels. It is through these that distant organs which, apparently, have no connection with the original focus of disease, become involved in the process.

Since I first showed the presence of characteristic manifestations in various organs, the brain, the heart, the spleen, the liver, and the kidneys, the existence of such metastatic formations has been understood without difficulty. Many other authors have confirmed these observations, the writer's explanation of which was that the appearances were caused by embolic processes. The appearance of the metastasis is always immediately and distinctly indicative of its

true nature, but it is not always easy to decide at once the relation between what appears to be the original focus and the metastatic deposit. We meet also with many intermediate forms of mixed infection, varying from the chronic, practically sterile pyæmic abscess to the well-marked pathognomonic lesion of actinomycosis. The latter, the tumor-like metastasis, sometimes of a gelatinous consistence, consists of fleshy or fat-like masses much resembling gummata. No matter in what direction the section may be made, the same gelatinous quality is evident, often with a very characteristic honeycomb appearance, and in various parts of the mass we see spaces containing granules, and collections of the actinomyces intermingled with greenish pus.

Pathological Anatomy.

In agreement with the possible modes of entrance of the infection which we described in the preceding section, we differentiate a corresponding number of pathological anatomical forms. We may exclude from this arrangement a number of cases representing various stages of transition between actinomycosis and some slow forms of pyæmic processes.

Actinomycosis of the Head and Neck.

1. To this division belong the frequently observed spongy or gelatinous nodules with abscess and fluctuation in the neck, which are so often associated with fistula formation. In this division may be placed also cases of the disease in the upper maxillary, facial, and mastoid regions.

2. Cases with the disease in the inferior maxillary region, including involvements of the tongue, floor of the mouth, and chin.

3. Cases involving the neck and paracesophageal and prevertebral tissue with mediastinal disease in some cases.

Actinomycosis of the Air Passages.

(Primary Actinomycosis of the Lungs.)

This shows itself in a chronic thickening of the lung tissue, starting in many small areas of consolidation of peribronchial origin.

In this focus or area, which gradually increases in size and involves more and more of the lobule in which it is, there is a progressive sclerosis of lung tissue and extension of the disease. Whether there is local disease at many points, or whether there is a single large circumscribed area, this infiltration or sclerosis accom-

panies a microscopic breaking down of the tissues involved. This sort of breaking-down process often furnishes the starting-point of those extensions in the bronchial system by which the actinomycosis is disseminated through the lobule in question. In a very interesting case reported by Israel, the carrier of the infection was a piece of a carious tooth found in the midst of an area of broken-down inflammatory products in the lung; and it is from just such processes that the beginnings of what eventually become large cavities, involving almost the entire lung, may arise and make the clinical picture one closely resembling tuberculosis. Extension of the inflammation to the pleura furnishes the preliminary, after which the disease reaches the connective-tissue layers, and gives rise to those characteristic formations, gelatinous or more dense and cicatricial, which appear behind the pleura or along the ribs. In this manner the process usually spreads often along the left side of the œsophagus, sometimes but more rarely on both sides of the thoracic vertebræ, until the whole region is involved in the disease and the tissues are riddled with the characteristic sinuses. The soft, spongy layer thus developed in the superficial tissues, perhaps several centimetres thick, envelops the lower and posterior parts of the involved lung and gives passage to the fistulous tracts, many of which open between the scapula and spinal column. The picture is thus one of a chronic parapleuritis or of a retropleural phlegmon.

Actinomycosis of the Digestive Tract.

The disease appears at various places in the stomach and intestine, especially in the small intestine. From these points the process extends to the iliac fossa and also other sections of the peritoneum. When there is preliminary adhesion of the diseased portion to any part of the abdominal wall, the outbreak of the disease manifests itself at such a point, sometimes directly, or sometimes by burrowing beneath Poupart's ligament, or even on the anterior surface of the thigh at the level of the lesser trochanter. In other cases the formation of peritoneal adhesions allows the process to involve the liver or the ovaries and tubes.

Actinomycosis of the Skin.

If we except those cases which start from infection from the mouth, we shall find that the skin of the rest of the body is very rarely affected by actinomycosis. There remains a fair proportion of cases in which at autopsy it is impossible to determine the point of inva-

sion of the disease, and such cases might perhaps be placed in a group by themselves.

Among 421 cases of Illich,[15] there were 51.8 per cent. localized in the neck, or, including the tongue, 55.5 per cent., 13.8 per cent. in the lungs, 21 per cent. in the abdomen, 2.6 per cent. in the skin, and 7 per cent. with the location undescribed.

Symptoms.

Actinomycosis is at first a local disease, and is of slow development. This fact is important in respect to prognosis and treatment, and likewise emphasizes the fact that we should attend to the removal of the local infection at the earliest possible moment.

Actinomycosis, then, appears to us a chronic disease with an extraordinarily insidious and prolonged course. The initial stages are usually so obscure that the true nature of the disease frequently remains undiscovered for a long time. This peculiar indefiniteness of symptoms and slowness of progress, seen in very few diseases, and the fact that the disease is not limited to any particular organ, help to make up the clinical picture of this unusual affection. We may first see something characteristic of actinomycosis when there is some external objective manifestation, after a longer or shorter period, perhaps when the disease has run half its course, in the region of the jaw and side of the head or neck, or in the more obscure region on either side of the vertebral column along the œsophagus or more posteriorly, or in some cases in the iliac fossa and perineum, or on the anterior surface of the thigh. There are very few portions of the human body which may not be the seat of the actinomycotic process, and almost no organ which may not furnish lodgment for its primary focus.

From all the facts which we have mentioned we may deduce a comprehensive description of the course of the disease. We must remember that the invasion of actinomycosis and its extension from its original focus may occupy such a long time, and may involve so many organs that the whole clinical picture is that of chronic pyæmia, for which it may be mistaken.

Head and Neck.—The tough quality of the infiltration in those cases involving the external parts of the body, especially the head and neck, with the tendency to extension by burrowing, is characteristic of many cases.

Lungs.—Actinomycosis of the respiratory passages runs its course usually with the appearances of a chronic inflammation of the lungs, which here and there shows a tendency to softening and the formation

of cavities, and is often accompanied by symptoms which closely resemble those of emphysema. We also see symptoms referable to pleural irritation and cough, often with free expectoration. The latter is sometimes mucopurulent, sometimes mixed with blood, and occasionally putrid. The presence of actinomycosis granules in the sputum is, however, not invariable; although it would be expected from the condition of bronchopneumonia with inflammation and degeneration found at autopsy, and with the spots of softening and breaking down of lung tissue so near the bronchi, that the expectoration would regularly contain such evidences of the disease. In thirty-four cases of pulmonary actinomycosis, recently collected by Hodenpyl, we find only nine instances in which the disease was shown by the sputum. In nine other cases it was possible to find the fungus in the pus discharged from the sinuses in the chest wall, while in the other cases the search was in vain, or was not made. In addition to cough and expectoration, fever is the most important symptom, and is usually irregular in type. Just as is usual in the later stages of tuberculosis, we see the emaciation and the exhausting night sweats and other appearances of pulmonary consumption.

If the fever assumes a more and more hectic character, the disease may drag itself along through months or even several years, until general exhaustion or the occurrence of complications, such as tuberculosis or amyloid degeneration, endangers the patient's life. With the signs of increasing pulmonary involvement, we soon have the evidences of pleural inflammation, sometimes very prominent, sometimes obscure, with the formation of more or less dense or fatty tissue. Numerous sinuses and fistulæ may form with the extension of the causative infection. This tissue, often very thick and strong, may extend directly into the mediastinal or prevertebral spaces, or into the retropleural region, and when the slowly increasing and extending fistulæ have finally formed external openings through the soft parts of the back we have a system of communicating passages running from the crater-shaped sinus openings to the gangrenous tumor formations in the lungs or elsewhere in the thoracic cavity. In many cases in which the examination of the sputum has been negative, a methodical examination of the pus in the proper way may be useful.

Intestine.—Still more difficult is it to make a diagnosis in the case of intestinal localization. The diagnosis is often clear only when the destructive process in the intestine has reached and involved the abdominal wall. Usually the destructive process extends so slowly from the portion of intestine immediately involved that the neighboring coils have time to become adherent to each other and thus protect the general peritoneal cavity. Thus our first correct idea of the disease

may be got from the opening through the abdominal wall made possible by the formation of adhesions. In consequence of this involvement of the abdominal wall, we find developed a hard mass of characteristic infiltration with sinus formation, the discharge from which gives us the first accurate information as to the character of the disease. Not uncommonly the lesion "points" in the lumbar region like a paranephritic phlegmon, or like an abscess coming from disease of the appendix pointing in the lumbar region, or a psoas abscess. Since the actinomycotic swelling has a tendency to extend farther and farther from its original focus, even as far as the trochanteric region, the resemblance to the abscess of vertebral origin is still more marked. Similarly but more rarely the external opening may be in the gluteal or perineal region. Sometimes the collections open into sacculations in the abdominal cavity, thereby causing a progressive chronic peritonitis which may involve other regions of the abdominal cavity or of the intestine, or may open into the bladder or any other abdominal organ. Under all circumstances the course of the disease is that of a sacculating peritonitis whose diagnosis has long been one of the most difficult, unless we can get some such aid as that afforded by the presence of the fungus granules in the discharge.

Skin.—Actinomycosis involves the skin very rarely. Sometimes, however, we see it in the form of small, fungous growths, sometimes in the form of granulation masses, sometimes in that of crater-shaped ulcerations. In other cases the eruption appears more like disseminated nodules which are healing in the centre and ulcerating at the periphery. In any case there is at the same time either an infiltration or a sclerosing involvement of the subcutaneous tissue. In such cases the treatment of single masses is of so little avail that the removal of even a large number of them does not in any way prevent the growth of more, and the continued progress of the disease.

Diagnosis.

Since the significance of the ray-fungus granules has been known, and since their causative rôle in exciting the growth of certain granulation tissue and the formation of pus foci has been decided, the diagnosis of actinomycosis may be considered easy.

If by chance even with such an important diagnostic aid we meet with difficulties in deciding, the proof will rest upon the kind and number of external manifestations of the disease which appear, and the limited number of regions of the body in which it is localized. A hardly less important hindrance to an early definite conclusion

consists in the length of time which may elapse between the exposure to infection and the beginning of the disease. In consequence we should never neglect to examine for actinomycosis with great care in all cases of a doubtful nature characterized by the presence of granulation tissue, fistulæ, and abscesses.

Prognosis.

Since the removal of all parasitic germs forms the preliminary to the successful treatment of the disease, it is clear that this must depend upon the accessibility of each focus and its associated extensions. As long as these foci are on the external aspect of the body, and are accessible to surgical treatment, we have every prospect of overcoming the disease. As soon, however, as the ray fungus has penetrated into the deeper portions or into one of the great body cavities, the danger at once arises that one or more of the viscera may be invaded to such an extent as to endanger or destroy life by the generalization of the disease. The more an organ is invaded, the greater becomes the danger of the disease breaking into the vascular system. Such an occurrence means the unlimited spread of the actinomycosis germs, and thus the impossibility of freeing the body from them.

Treatment.

Although Billroth and Illich claim to have seen a reaction in actinomycotic patients from the injection of Koch's tuberculin, such as is seen in tuberculosis, I have not been able to confirm these observations. In the case of a supposed consumptive, although the reaction remained absent, I found at autopsy the lungs destroyed by actinomycosis instead of by the expected tuberculosis. Any favorable action of tuberculin in the cases mentioned by Billroth and Illich must be accepted with reserve, since both cases were treated surgically, and surgical measures alone not infrequently lead to cure. The superficial localization in the maxillary region and in the face offers favorable conditions for treatment, and we may open the tumors, empty them of their contents, and treat them and the fistulous canals by scraping away all the granulation tissue, with the addition of subsequent drainage. This is usually sufficient to prevent local recurrence. Those less well-circumscribed and more indurated swellings which have the characteristics of infiltrations show greater resistance. For such cases it is a good plan to use injections of 1:500 bichloride-of-mercury solution repeated several times, instead of the boric-acid injections formerly employed. When the disease is well advanced and there

are metastatic involvements, we must proceed according to the general rules of surgery, at the same time that careful attention is given to any appearances of increasing general infection, to the occurrence of fever, or to any effect on the general condition of nutrition.

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RABIES.

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RABIES.

Synonyms.—Lyssa, Hydrophobia; Fr., *Rage;* Ger., *Hundswuth, Wasserscheu.*

History.

Democritus of Abdera, the so-called laughing philosopher, in the fifth century B.C., is accredited with the earliest account of rabies. He regarded it as an inflammation of the nerves, a severe, spasmodic disease, like tetanus. It did not excite his risibility either derisively or incredulously. His opinion was like that of Celsus, who (B.C. 21) wrote: "It is a most miserable kind of disease, in which the sick man is at the same time tormented by a dread of food and water, in which condition hope is reduced to a narrow limit." Aristotle (fourth century B.C.) refers to rabies in the dog and its transmission to other animals when bitten. Hippocrates, contemporaneous with Demetrius, makes no mention of rabies, not because he did not know of it, but no case was in his personal knowledge. Unlike philosophy, medicine cannot dispense with experience. For like reason Trousseau (1850) discusses the disease, but Graves (1848) does not. The description of the former is unsurpassed in the vivid actuality with which the clinical phenomena are presented. It was reserved for Pasteur, in 1882, to treat the disease with definite scientific accuracy.

Ancient Authorities.—Many of the ancient classical writers, historians, philosophers, poets, and physicians refer to rabies. Xenophon, 445 B.C.; Ovid, 107 B.C; Virgil, 70 B.C.; Horace, 65 B.C.; Plutarch, first century; Galen and Cœlius Aurelianus, 131 A.D.; the former styles rabies the worst of all diseases. Rhazes (922 A.D.) and Avicenna (1036 A.D.), and succeeding authors contributed nothing of importance to our knowledge of this disease.

Early Modern Authorities.—Centuries elapsed before the earlier modern writers resumed the investigation of rabies. Boerhaave (1700 A.D.) and Van Swieten (1771 A.D.) refer to pain in the bitten part and neighboring regions as premonitory, which sometimes like an aura radiates along the nerves. The latter makes the important observation that in a case of rabies in man "death was not preceded by convulsions or struggles, but as if universal paralysis caused death."

John Hunter (1776) is responsible for the statement that only five per cent. of those bitten became rabid. Magendie and Bouchet (1813) "produced rabies in dogs by inoculating the saliva of a rabid man, afterwards the experiment was confirmed by Reynault at Alfort." Marochetti of Moscow (1820) asserts that in all cases in which medical treatment has not been early applied small knots appear under the tongue at the openings of the submaxillary glands, and that by the use of a probe a fluctuating fluid, which is the hydrophobia poison, may be perceived. Fifteen cases came under treatment on the same day and twelve exhibited the knots. They usually appeared within the third and ninth days after the bite. Marochetti examined the mouth once or twice a day, and as soon as these knots or pustules appeared they were opened and cauterized with a red-hot needle; after which the patient was made to gargle frequently with a decoction of broom. If the knots were not opened within twenty-four hours the poison was reabsorbed and the patient died. Thirty-eight patients were thus cured. Sixteen were well three years afterwards (*Westminster Review*, 1824). Morgagni doubted the efficacy of the above-described treatment. Trousseaux, as late as 1861, regarded these statements as worthy of attention. Dupuy (1824) states that uniformly he has found the spinal cord softened, diffluent, and of a deep yellow color, especially in its lower portion. Youatt (1850), who is reported to have relied on nitrate of silver as a caustic, is said to have been bitten seven times with impunity, and finally to have died of this disease in spite of his own remedy. M. H. Bouley records that only twenty or twenty-five cases of rabies occur annually in a population of thirty-six millions. Watson (1885) asserts that the Earl of Richmond died of rabies from the bite of a tame fox. Virchow and von Ziemssen (Bollinger, "reject the theory of spontaneous development" (1875). During this period it was already known that the saliva or the nervous tissue, hypodermically introduced, could propagate rabies from man to the lower animals as well as from these to one another.

Recent Modern Authorities.—The epoch of recent accurate investigation dates from 1880. It may be regarded as the capstone of Pasteur's mental monument. Around the shaft are imperishably engraven the names of Roux, Chamberland, Grancher, and as the master desired, that of Thuillier, who, before its completion died of cholera in Egypt; Duclaux, founder of the *Annales de l'Institut Pasteur* and since 1895 Director of the Institute; Metchnikoff, Director of Bacteriological Department, Nocard, Babes, Strauss, Calmette, Yersin, Gamaleïa, and Galtier (1881). The book of Renaud Suzor in English (1887) is an admirable presentation of the whole subject at that date. Victor Horsley's experimental demonstration of rabies

in the deer of the English parks is an example of accurate work. In Italy were Tizzoni, Cantani, and Bruschettini.

Geographical Distribution.

The regional prevalence of rabies is a field fertile in ill-ascertained, conflicting assertions. Virchow is inclined to regard Greenland, Denmark, the whole of Africa, and parts of Asia and South America as exempt. Bondin (1861) thinks it rare in the tropics. In 1860 it was epizootic in Greenland while the temperature was at 25° below zero. In Constantinople, often referred to as free from the disease, it prevailed extensively in 1839. It occurs in Egypt notwithstanding the denial of Larrey. "In Missouri and Ohio, in 1860, so many cattle were destroyed by this disease that the owners sought reimbursement from the government." It is said to be rare in California. In London between 1603 and 1728 no cases are noted in the mortuary statistics, subsequently cases are regularly reported. In Hamburg it was epizootic from 1851 to 1856, when 600 authentic cases occurred. In Saxony between 1853 and 1867 there were 807 genuine or suspected cases. In Bavaria from 1863 to 1867 among 275,000 dogs there was a yearly average of 800 cases, genuine or suspected. The foregoing account is from Boulanger, who asserts in italics that no land or country is free from hydrophobia.

The seasonal prevalence of rabies is assigned by vulgar belief to mid-summer or dog-days; probably an outcome of association with the ascendency of the dog star (Sirius). "In respect to the seasons, no very decided preference is evinced for any particular period. It may rage at any time, but appears to be slightly more prevalent during the spring and summer months" (Bollinger[1]). The appended table from Suzor does not bear out this statement as regards summer months:

June, July, and August	14
March, April, and May	35
September, October, and November	25
December, January, and February	14

Within my own knowledge two cases occurred in February, one in January, three in December. There is some evidence that prolonged heat may prolong the incubative stage, and some that it may postpone the time of death. J. M. Byron[2] states that a cord in the incubator at 40° C. for eight days produced when inoculated into rabbits marked symptoms of rabies, but the animals did not die. "Moderately high temperatures, acting in experiments in tubes, have an attenuating in-

fluence on virulent cords; atmospheric temperature influencing inoculated animals seems to affect the virulence, but further experimental data are needed before deriving any definite conclusion." Dr. Acosta, of Havana, reported to Dr. Byron the same irregularities in experimental rabies during the hot summer months.

RABIES IN ANIMALS.

The animals subject to rabies are among the Omnivora, Carnivora, Herbivora, Rodents, and it is asserted Saurians and Batrachians, these perhaps without adequate proof: man, dog, cat, horse, cow, sheep, goat, swine, deer, wolf, jackal, and allied species. Rabbits and guinea-pigs are the experimental subjects of this disease. There is no mention of its prevalence among lions, leopards, or wildcats, but it is probable that the disease could be experimentally conveyed to them. It can be so transmitted to the domestic mouse, which is very susceptible to the disease. It exhibits the signs markedly. The disorder of motility is very evident when this active little animal is so situated as to enable it to exercise freely. A small cage with a compartment opening into a light tin and wire bar wheel so constructed as to revolve easily affords the mouse an opportunity to display its agility. It delights in turning the wheel, which it does rapidly and with exact coördination, never missing to place its foot upon the bar. The onset of rabies is shown in the slower movement, in missing the bar, in thrusting its extremities between the bars, and stopping often to rest. From this condition the disease develops in the direction of quiet or of excited rabies. In the former the mouse tends to rest. If undisturbed the disease is not evident, there being only a degree of tremor; but, forced to move, the usual incoördination becomes manifest. It attempts to revolve the wheel, frequently missing the bar. At a further stage it turns the wheel with its fore limbs, the hind ones being extended, motionless, and dragged outstretched backwards, paralyzed. In the excited form there is a tendency to restlessness; slight disturbance causes it to stagger from one compartment to the other. It struggles to revolve the wheel, falling from side to side and over and over. Recovery even in this advanced stage is not impossible in the mouse. In the rabbit it has not been observed to occur when the symptoms have fully declared themselves.

So characteristic are the signs of this disease in the mouse that, except for the purpose of exhaustive demonstration, the transfer from mouse to rabbit is supererogative. It is readily transferable as the experiments cited below abundantly demonstrate. The mice received injections into the subcutaneous tissue at the root of the tail. A piece,

2 cm. long, of the medulla oblongata of a rabid rabbit, was rubbed up in 1 c.c. of bouillon. Of this five minims were injected into the back at the junction of the tail, with an ordinary hypodermic syringe. In the return control experiments the medulla oblongata of these mice, in which the disease had been experimentally produced, was used to inject the trephined rabbits subdurally.

The source of the material in all cases except three was the medulla oblongata of rabid rabbits. In these three exceptions, in which rabies did not develop, hypodermic injections were made of material from the medulla oblongata of a rabid hen, from the medulla of a rabid mouse, and from a culture from the medulla oblongata of a rabid man. Rabic virus in a hen having a temperature of 108° F. becomes sterile, and cases of cultures from it producing rabies are unknown, so that one of these cases must be classed with accidental deaths. The total number of mice was 31: Accidental deaths, 8; regular rabies, 17; recovered, 1; convalesced and relapsed, 1; escaped the disease, 4. Subtracting accidental deaths from the total reduces the number to 23—19 of which took rabies. If this is a maintainable average, then 82 per cent. of mice take the disease when hypodermically injected.

As a control to these experiments 17 rabbits were trephined and inoculated with the medulla oblongata of the rabid mice and all died of rabies. Of these several are noteworthy. Rabbit No. 147 was trephined and injected subdurally with some of the medulla of mouse No. 6 rubbed up in bouillon. Mouse No. 6 had been injected at the root of the tail hypodermically with the medulla of rabbit No. 121, and developed rabies on the ninth day. Rabbit No. 140, injected subdurally from mouse No. 2, developed rabies on the ninth day. Rabbit No. 118, trephined from the medulla of mouse No. 1, had advanced rabies on the eleventh day; mouse No. 2, injected hypodermically from the medulla of this rabbit, developed rabies on the eighth day. Rabbit No. 117, injected subdurally from the medulla oblongata of mouse No. 1, had advanced rabies on the eleventh day.

Experimental Inoculation.

The presence of rabies in an animal and the susceptibility of an animal to rabies must be experimentally demonstrated. The material preferably used is a portion of the medulla oblongata of the suspected animal, which is introduced by injection beneath the dura mater. The anterior chamber of the eye may be used, the ear vein or some other vein, or the nerves. The surest method, very rarely failing, is injection into the subdural cerebral lymph space. This involves perforation of the skull, which is usually done by tre-

phining. Pasteur invented this method, without which failure to inoculate is so frequent that experiments frequently miscarry. It is claimed that only two-thirds of the animals artificially inoculated by other methods with saliva take the disease, which is also the proportion when dogs are bitten by rabid dogs (Youatt). From causes that cannot be explained hypodermic inoculation often fails. Nine attempts by Hertwig to inoculate a poodle failed. Pasteur observed this natural immunity, and asked: "Are any dogs refractory to rabies, or have those apparently so had a mild attack and recovered? Dogs and rabbits may have a mild attack and recover, but never after the advent of acute symptoms." "We at present have in our possession four dogs which are not susceptible of taking rabies whatever method of inoculation be used and whatever also the virulence of the rabid material employed."

Method of Trephining.—The appliances for trephining are a board 77 cm. long by 36 cm. wide having two holes at each side of either end 7 cm. apart and of 1½ cm. diameter. Through these apertures narrow flat or round leather straps are passed and secured, having previously been fastened to the legs by a slip knot. The board previously described has strips fastened to the bottom so that it is elevated above the table on which it is placed; the strips are 12 cm. high. The zinc or slate-covered dissecting table is convenient to place the rabbit board upon. A smaller board, 60 by 36 cm., is used to hold the instruments. The straps should be placed on the legs first, then the hind legs fastened to the board; up to this point the rabbit has not been disturbed and remains quiet. Now the straps on the fore legs are seized and the rabbit is stretched out by pulling on them, after which they are passed through the orifices and made fast. The hair between a line drawn transversely through the ears and eyes is cut off with scissors and the skin is washed with a three-per-cent. solution of carbolic acid. No anæsthetic is required; the animal does not cry out and evinces no sign of pain. A cut one inch and a quarter long is made with the knife or scissors, longitudinally, through the skin in the middle of the space at the top of the head between the lines above named. A blepharostat keeps the incision apart, and the sublying tissue is scraped away so as to expose the bone a little to one side of the median line. The trephine has a diameter of 5 mm. and a ring guard which is set at 2 mm. from the cutting end of the crown; the trephine may be a bit fastened in a revolving drill handle or a simple hand trephine made of metal rod 17 cm. long. The button of bone is removed with a tenaculum and the dura is exposed; an ordinary hypodermic syringe is used to inject three or four drops of the rabic emulsion beneath the dura. If the perforating end of the syringe is

curved almost at a right angle for a space of 4 mm. it facilitates its introduction, but this is by no means indispensable. The wound is closed by interrupted sutures (three generally are sufficient) and then sealed with collodion. The ordinary suture needle can be used, but the risk of sticking the hand is lessened if the needle has a fixed handle, the other extremity terminating in a spear with a slit in its side, which is opened and closed by pushing a button. It is passed through the skin closed, then opened, and the thread is inserted, when it is again closed and withdrawn. Of course, all the materials and instruments have been sterilized and when not in use during the operation are placed in a pan of three-per-cent. carbolic acid. The rabbit is lifted by the skin of the middle of its back, raised somewhat from the board, and the fore limbs are loosened first. The rabbit is then placed in a box properly labelled. Wire cages are generally used, but if the floor is of asphalt or other cement, a box without a bottom having a wire grating for a lid with a bed of sawdust or straw is more convenient to keep clean.

Etiology.

The intimate cause of rabies remains unknown to this day. Notwithstanding the constant, ample supply of material, research is still at fault. Pasteur himself, for a brief time, thought that he had discovered the bacillus of rabies in the saliva of a child that had died of this disease. The disease produced was septicæmia, as finally determined, but pending this Pasteur "expressed the idea that this new disease might possibly be the form assumed by human rabies in the lower animals" (Suzor[3]). A. Bruschettini,[4] of Turin, claims to have discovered the cause of rabies in a small, short, thick bacillus with a clear zone in its centre. A bacillus of this description may be found in the medulla oblongata of rabid dogs, and this grown in emulsion of the brain, removed, and regrown to the fifth generation is claimed to have produced rabies in subdural inoculations of rabbits, and the brain matter of these to have in like manner produced this disease in other rabbits.

G. Memmo,[5] of Rome, claims to have discovered the cause of rabies in a species of blastomycetes from the brain of experimentally rabid rabbits, also from the brain of a child that had rabies from a dog-bite. "This organism intraperitoneally injected into guinea-pigs in eleven to twenty days causes paresis of the hind limbs, extending rapidly, and death in about twenty-four hours, often preceded by clonic convulsions. The virus from the abdominal cavity produces some symptoms in other guinea-pigs. Dogs injected subdurally or subcutaneously become thin in seven to eight days, snappy,

foam at the mouth, and are paralyzed in the limbs. This disease could be transmitted from dog to dog but not to guinea-pigs" (Gorman Sims Woodhead[6]). Both of these investigations cannot be right, and neither has received general scientific confirmatory demonstration and acceptance. The bacillus described by Bruschettini is like that of rabbit septicæmia, except that it is coarser, which the bacillus of rabbit septicæmia also becomes when grown in certain media. Many of these bacilli with clear centres and bipolar staining are decomposition organisms, the clear centre being a gas vacuole, and sometimes a surrounding clear space of like nature deceptively resembles a capsule. It has been suggested that rabies is a modified septicæmia with a predilection for the nervous system. The writer has never been able, except in the case of one rabbit, to get a prolonged incubative stage like that of rabies in experiments with septicæmia virus; moreover, in this case all the symptoms so characteristic of rabies were not present.

That the well-known bipolar staining bacillus of rabbit septicæmia may be found in the medulla oblongata of a supposed rabid dog the following experiments demonstrate. In the course of an investigation regarding the etiology of rabies it became necessary for the purposes of control to use the medulla oblongata of a number of dogs for subdural inoculation. One object of these controls being the determination as to whether any other disease than rabies could give rise to like symptoms, it was requisite to use sick dogs; therefore the dogs used had died or had been killed because of suspected rabies. The bacteriological developments of dog No. 17 are noteworthy. This dog was a yellow cur weighing twenty pounds that had attempted to bite a number of persons; it bit other dogs and took refuge in a stable and there bit a horse. It was shot.

Post-mortem examination, September 22d, 1893: Inspection, skull crushed and brain torn; mouth pigment present (a sign of no value as regards rabies, for dogs' mouths are often pigmented). Cheeks and surface of tongue bluish vascularity. Bits of coal and splinter in the under mouth (a sign of not much value in a dog that obtains his sustenance from the garbage box). Section: cervical lymph glands enlarged and blood effused into them. This sign is important as indicating toxic infection, and is present in rabies in the lymph glands at large in the body, macroscopically or microscopically. Medulla oblongata under surface very vascular. Larynx somewhat red, and the mucosa of the laryngeal ventricles protrudes. Œsophagus pinkish; stomach contains hair, straw, grape skins, feathers. Heart blood coagulated. Lungs ooze a sanious serum. Liver hyperæmic. Spleen

reddish, firm, weight 19.4 gm., length, 16 cm., width at wider end, 4 cm., at other end, 1 cm., thickness, 5 mm.

Cultures from the medulla oblongata, spleen, lymph glands, and parotid were grown in gelatin. Cultures from the cervical lymph gland in bouillon were placed in the thermostat.

September 24th, 4 P.M.: Gelatin liquefied contaminatively (which the organism about to be referred to does not do). Cultures in bouillon are very fetid and exhibit lance-shaped cocci (bacilli); also bacilli with clear interspace and bipolar staining, and curved chains of five or six. There is also a short, thick bacillus in gas vacuole, which is present in ordinary putrefaction. The cultures from gelatin are less gross than those from bouillon and exhibit more clearly the unstained intermediate space. The odor of the gelatin cultures is as fetid as those in bouillon. The above applies to the cervical lymph glands of dog No. 17, and to the heart blood of rabbit R in gelatin, below referred to (rabbit R was trephined and inoculated from the medulla oblongata of dog No. 17). This bacillus, slender, with rounded ends, bipolar staining, and clear interspace, varies in size in the same media, differs in size in different organs and structures. It is the well-known bacillus of rabbit septicæmia, and further reference to its morphology and mode of growth is out of place on this occasion. Lenses of good definition are indispensable, because the organism is often very short and the clear interspace very narrow, easily mistaken for juxtaposed cocci. The ordinary carbol-fuchsin stain, if allowed to remain but a few seconds on the cover smear, gives satisfactory results. The following are the details of this experiment:

On September 22d, three rabbits were trephined and injected beneath the dura and three were injected hypodermically in the lumbar region with the medulla oblongata of this same dog. These rabbits were designated K, T, and W, the trephined rabbits by the letters R, W, and X. Rabbit R died on the third day, rabbits W and X on the second day. Rabbits K and W died on the second day and T on the fourth day. Cultures from the heart blood of all these animals exhibited the organism described above. Cultures from the heart blood of rabbit R, which was trephined and inoculated from the medulla oblongata of dog No. 17, injected hypodermatically into rabbit Y killed it in one day. Cultures from the heart blood of rabbits K and T (which rabbits were directly injected with the medulla oblongata of the dog) killed rabbit T′ in one day.

Referring to the post-mortem examination of dog No. 17, it will be noticed that its cervical lymph glands were enlarged and blood was effused into them. Cultures from the glands gave the following interesting results: 1 c.c. of the bouillon culture injected into rabbit Z

killed it on the second day; this was the first remove from the dog. Cultures of the heart blood of rabbit Z in Dunham's fluid injected into rabbit Z′ killed it on the second day. Rabbit T′ was identically injected and also died on the second day. These rabbits were second removes from the dog. Guinea-pig H, injected with 1 c.c. of a culture of the heart blood of rabbit Z in Dunham's fluid, died on the sixth day. Guinea-pig G, injected with 1 c.c. culture of heart blood of rabbit Z in gelatin, died on the sixth day. These guinea-pigs were second removes from the dog. Mouse A, injected with five minims of culture of heart blood of rabbit Z in Dunham's fluid, died on the third day. This mouse was the second remove from the dog. Cultures from the heart blood of the mouse A in Dunham's fluid injected into rabbits S′ and L′ killed them on the third day; this was the third remove from the dog. Cultures from the heart blood of guinea-pig G (above mentioned) in Dunham's fluid injected into rabbits R′ and Q′ killed them on the second day; this was the third remove from the dog. Cultures from the heart blood of this same guinea-pig G injected into pigeon A killed it on the seventh day; this was the third remove from the dog. Rabbit N′ was injected with the culture of the heart blood of pigeon A and died on the second day; this was the fourth remove from the dog. The experiment ceased with the fourth remove from the dog. Another pigeon (B) was killed by an injection of the culture of heart blood, this being also the fourth remove from the dog through mouse A. All of these animals, as well as the cultures, exhibited the organism described above. Two white rats, three times injected, remained immune. It is to be noted that when other animals than rabbits have been killed by culture, other rabbits have been killed by cultures from these animals, constituting a return control experiment.

The symptoms of septicæmia in the rabbit ante mortem and post mortem are markedly characteristic and can never be confounded with those of rabies. The ante-mortem signs are somnolency and dyspnœa. The animal sits with its ears turned back upon its body, its flanks panting laboriously, its eyelids constantly closing. The alvine evacuations are pultaceous. The temperature may rise to 106° F., which is one or two degrees above the normal maximum; this rise is very transient, rapidly falling three degrees below the normal temperature of the rabbit; the normal minimum temperature is about 100° F. Usually these animals die quietly; exceptionally, convulsed. A constant post-mortem sign is the pale, salmon colored, bloodless, anæmic, collapsed lung. The spleen is sometimes enlarged; the liver friable. The intestine has exhibited no lesion except increased vascularity. The site of the injection usually shows

increased vascularity, exceptionally sloughing. Of great interest is the fact that this organism of rabbit septicæmia was obtained from the medulla oblongata of a probably rabid dog. Had these rabbits recovered from the septicæmia they would have died of rabies, and a causal relation might have been erroneously attributed to this organism.

The disease produced by this bipolar bacillus is totally unlike that produced by the virus of rabies. The incubation in rabies, even when the virus is fixed, is six days. The rabbits infected with the septicæmia organism became sick in a few hours and died about the third day. Rabbits with rabies from the dog immediately without intervening experimental transmission do not exhibit rabies until from the twelfth to the fifteenth day, usually the latter. Rabid rabbits survive three, four, and five days after the development of the disease. Muscular incoördination and paralysis are marked in rabies; they are absent in septicæmia. There is, however, a disease known as pseudo-rabies, in which the incoördination and paralysis are exactly like those of true rabies, and may, like true rabies, be produced by subdural inoculation of the medulla oblongata. This is also an idiopathic disease of rabbits and may supervene without inoculation, so that a confusion of causation might arise during experimentation. But inoculation of the rabbits would be followed by the characteristic short incubation and easy cultural reproduction.

Though the *causa causans*, the ultimate cause, of rabies eludes detection, the proximate cause is readily demonstrable and can be indefinitely propagated experimentally. When naturally imparted there is a tendency to extinction. "Magendie got a first mad dog to bite a second healthy one; this in turn, when mad, a third one, and so on. The periods of incubation became longer and longer and the fourth or fifth dog failed to take the disease" (Suzor). Galtier (1881) produced rabies in rabbits by the insertion of pieces of the brain and medulla of rabid dogs under the skin. That the cause of hydrophobia is seated in the nervous system is constantly proven. Especially is the medulla oblongata virulent, and this is the part used in experimental inoculation. The Paris virus from the Institut Pasteur in use at the laboratory of the College of Physicians and Surgeons, in Baltimore, was received in neutral glycerin, which is said to impair its virulence for only the first two or three passages. This has not been my experience; the virus in glycerin seemed inert on one occasion and failed to produce rabies in three rabbits trephined and inoculated therewith. There is difficulty in fixing the virus when in this menstruum, and this has also been the experience in the New York Board of Health laboratory. A series of very interesting experi-

ments upon the frequency of rabies in the human made by the late Dr. J. M. Byron of the Loomis Laboratory, New York, has this element of vitiation, and in addition there seems to have been a bias in the direction of infrequency. This experiment shows that decomposition exerts little or no influence on rabic virus. Cords in an early stage of decomposition, when nothing is grossly noticeable except a little softening, promptly kill when inoculated subdurally or hypodermically. But the same nerve matter when stinking rotten may often be used successfully in imparting rabies. The Paris virus at the Baltimore laboratory at this date, May 30th, 1898, has reached the four hundred and ninety-ninth remove, that is, it has been passed from one rabbit to another until it has reached this number of passages; but as two rabbits are inoculated subdurally each time, it has given this disease to at least nine hundred and ninety-eight rabbits. This Paris virus started from the medulla oblongata of a rabid cow in 1882. Another virus in use at the same institution was introduced by the writer October 5th, 1893. Coincidentally, this virus also started with the medulla oblongata of a rabid cow received from Wm. R. Tatum, D.V.S., Brighton, Md. This virus has been passed from rabbit to rabbit until one hundred and fifty-three removes have been reached (May 30th, 1898). The number of rabbits that have uninterruptedly taken this disease in these experiments is seven hundred and sixty. In the earlier experiments more than two rabbits were used at each subdural inoculation. A rabbit will live about twelve days after inoculation, so that about thirty passages may be made each year. Inoculating with the medulla oblongata of a rabid horse the disease has been passed from rabbit to rabbit to the tenth remove. Sixty rabbits were the subjects of this experiment. The disease has been passed three times from the human animal to the rabbit, using in this experiment fourteen rabbits and stopping at the second remove. If a fixed virus were obtained starting from the medulla oblongata of a human being there would probably be no appreciable difference. The antitoxin of rabbit serum is stated to be more effective in immunizing rabbits than that obtained from a different species.

Rabies can be passed from man to the lower animals with ease. Contrary statements in standard works by reputable authors as late as 1888 are surprising. Not only can the materies morbi be readily passed from human beings to other animals, but the source of the virus can to a certain degree be determined; that is, whether the virus is a fixed laboratory virus or a virus immediately from the animal—"*rage de rue.*" This was the grave question that confronted Pasteur when the first death from rabies occurred during treatment by his method. The profession and the public knew that rabic

virus was injected hypodermically into patients. Dr. Peter, of Paris, demanded the closure of the Institute, declaring that this treatment produced rabies. When Louise Pelletier, aged ten years, died of rabies on the fourteenth day after termination of the treatment, having developed this disease eleven days thereafter, it became necessary to show whether she was killed by the treatment or by the disease. The demonstration of the cause from which the death of this child resulted, and its origination, was a matter strictly of experimental investigation dependent upon the following data: The virus, immediately from a rabid animal (the medulla oblongata being used) injected subdurally into the cerebral lymph space, produces rabies in the rabbit at or about the fifteenth day. The remote fixed virus of the laboratory produces rabies in about six days. An emulsion of the medulla oblongata of this child, subdurally injected into two rabbits, did not produce rabies until the eighteenth day thereafter. The medulla oblongata of these rabbits (they having been allowed to die and not having been killed), injected in the manner above described, into other rabbits, caused them to develop rabies in fifteen days. The cause, then, of this child's death was the virus of rabies as it exists naturally, not this virus as made more virulent by progressive propagation experimentally.

Two points in this case are noteworthy. The child developed the disease on the eleventh day after the termination of the treatment. It requires fifteen days after termination of the treatment to complete immunization; therefore in this child the full benefit of the treatment had not been received. Cases of this description cannot be strictly accounted failures of the treatment. The second factor requiring attention is that the virus was inoculated into two sets of rabbits. The first set, consisting of two rabbits, was inoculated from the medulla oblongata of the child. When these rabbits died a second set of rabbits were inoculated from them, because in the first passage of the virus from one species to a different species the period of incubation in the latter is not uniform, but is variable as to duration. In the passage through the second set the virus, passing from and through the same species, exhibits by its period of incubation its grade of virulence. In the words of Pasteur: "The method rests essentially on the following facts: The rabbit inoculated under the dura mater, after trephining, with the spinal marrow of an ordinary mad dog, is always affected with rabies, and takes the disease after a length of incubation averaging about fifteen days. After a number of passages through rabbits varying from the twentieth to the twenty-fifth, the incubation falls down to eight days, which remains the normal incubation time for the next twenty or twenty-five pas-

sages. Then it reaches an incubation of seven days only, recurring with striking regularity up to at least the ninetieth passage; at this point there is a slight tendency towards a shorter period of incubation than seven days." The ultimate diminution of the period of incubation seems to be six days. A fixed virus produces rabies in six days, when subdurally inoculated.

The following cases are recorded because of intrinsic interest; further, because they in some degree illustrate the rigorous, exhaustive causal demonstration that science demands.

These cases have been designated as the Baltimore cases of rabies. On December 1st, 1896, a large dog, cross between St. Bernard and mastiff, bit eight boys in Baltimore City Annex. Of these boys four died of rabies within thirty-six days after having been bitten and within nineteen days after the termination of treatment by the Pasteur method in New York. The bites were severe in character and situated on the bare face and neck.

1. Wilson, aged 11 years. Seat of bite on face over left eye. Not cauterized. Date of discharge, December 17th, 1896. Date of bite, December 1st, 1896. Date of first treatment, forty-two hours after bite. Date of death, January 5th, 1897, eighteen days after termination of treatment.
2. Perry, aged 16 years. Seat of bite on cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, seventy-seven hours after bite. Date of death, December 26th, 1896, eight days after termination of treatment.
3. Eppers, aged 15 years. Seat of bite, back of neck. No efficient cauterization. Date of discharge, December 17th, 1896. Date of first treatment, fifty hours after bite. Date of death, December 26th, 1896, nine days after termination of treatment.
4. Henry, aged 8 years. Seat of bite, left cheek. No efficient cauterization. Date of discharge, December 18th, 1896. Date of first treatment, seventy-seven hours after bite. Date of death, December 21st, 1896, three days after termination of treatment.

A boy named Kiel was bitten on the ear, but through an ear warmer, and therefore must be excepted from the class of bites on bare parts. All bitten on the bare face and neck died; all others escaped. They are:

5. Perry, aged 18 years, brother of No. 2, bitten on the arm.
6. Ashley, aged 10 years, bitten on arm.
7. Buhl, aged 14 years, bitten on arm.
8. Kiel, Joseph, aged 15 years, bitten on ear through an ear warmer.

The chief object of this reference to these cases is to illustrate by an actual example the experimental methods used to prove that the

dog had rabies, and that two of the boys, Henry and Eppers, also had it. In the other two cases a post-mortem examination was not obtainable. It is also intended to prove that the virus was from the dog and not from the treatment.

The following are notes of the post-mortem examination of the dog, December 2d, 1896: Cross between St. Bernard and mastiff: yellow with white neck; weight, over one hundred pounds; shot after having bitten eight boys, many chickens, and dogs. Hard palate dark bluish in color. Rigor mortis marked. Brain soft. Medulla oblongata soft, and softening around central canal of spinal cord. Lungs ooze freely bloody froth. Kidneys, dark red cortex. Bladder empty. Liver normal. Spleen normal. Stomach contains pieces of wood and stone, straw, horsehair—mane or tail. Larynx and trachea contain blood from wounds in mouth. Heart normal. There is an effusion of blood in the cervical lymph glands.

On December 2d, 1896, three rabbits were trephined and injected beneath the dura with three minims of emulsion in sterilized water of the medulla oblongata of this dog. These animals developed rabies, two on the 15th, and one the 17th, day.

December 19th, 1896: Killed one of the rabbits (designated C) on the seventeenth day after inoculation. Trephined and injected the emulsion of its medulla oblongata in sterilized water subdurally into rabbits D, E, and F. Amount injected, five minims. Rabbit D died accidentally. E and F developed rabies on the 16th day.

Thus five rabbits have been given rabies from this dog; three immediately from the dog, two from one of these rabbits, this rabbit having been killed in order to stamp a suggestion of putrefaction as a fallacy. The latter experiment proves the disease to be an infectious neurosis, not a traumatic degeneration.

The following experiment demonstrates that Robert Henry died of rabies. He underwent Pasteur treatment in New York, arriving there about December 4th, 1896, and returning to Baltimore on the night of December 18th, being then sick. He died of rabies, December 21st. He had been bitten on December 1st.

On December 21st, four rabbits were trephined and injected subdurally with emulsion in sterilized water of the medulla oblongata of the boy Henry. Amount injected, five minims. One developed rabies on the 14th day; three on the 15th day.

The following experiments demonstrate that the boy Henry died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit was a specific infection and not a traumatic degeneration (neuritis, ascending or descending).

January 7th, 1897, rabbit K trephined and subdurally inoculated

from medulla oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally inoculated from medulla oblongata of boy Henry on December 21st, 1896. Rabbit K developed rabies on the fifteenth day.

January 7th, Rabbit L trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896, developed rabies on the thirteenth day.

The rabbit assumes a crouched position. It is unable to sustain its body erect on pelvis and scapula. Motility of limbs impaired, hind legs almost completely paralyzed. Falls over on its sides at intervals. This crouched attitude (paralytic rabies) has been a characteristic feature of the disease in most of these rabbits.

Experiment demonstrating that the cord of rabbit G was not virulent on the ninth day, and therefore the virus with which G was inoculated subdurally was from the dog and not from the treatment.

January 7th, Rabbit M trephined and subdurally inoculated from medulla oblongata of rabbit G, which died on the seventeenth day after having been trephined and subdurally injected from medulla oblongata of boy Henry on December 21st, 1896.

Rabbit is very unwell, very thin. Sweats about muzzle. Breath fetid like gangrene. This is an intercurrent malady and has no connection whatever with rabies or with the experimental inoculation. It is an affection which occurs not infrequently among rabbits that have been subjected to no experiment. There is reason to regard the disease as infectious. It has diarrhœa as a symptom. There is no disturbance of motility. The rabbit was found dead on the ninth day.

Two rabbits, O and P, trephined from this rabbit, developed no disease whatever. They were under observation for three months. This proves that this disease cannot be communicated by subdural injection of the medulla oblongata; also that the medulla oblongata did not contain the virus of rabies on the ninth day, which it would have contained had the virus been that of the treatment.

Rabbit N was subjected to the same experiments as rabbit M, and died of the same disease on the eleventh day after trephining. It is to be regretted that no experiment was made to ascertain the condition of the medulla oblongata at this date, as regards the virus of rabies.

Rabbits M and N were in the same box all the time.

Experiments demonstrating that Conrad Eppser, aged fifteen years, died of rabies. He underwent Pasteur treatment from December 2d to December 17th, 1896. He died of rabies, December 26th.

He had been bitten on December 1st, and the post-mortem examination was made December 26th.

On December 26th, 1896, four rabbits were trephined and injected subdurally with emulsion in sterilized water of medulla oblongata of the boy. Amount injected, five minims. Rabbits designated by letters Q, R, S, T. They developed rabies on the sixteenth day.

The following experiments demonstrate that the boy died of rabies; that the source of the virus was the dog and not the treatment; that the disease in the rabbit is a specific infection and not a traumatic degeneration (ascending or descending neuritis). Rabbits U, V, W, and X were trephined and subdurally injected with emulsion of medulla oblongata, that of rabbit S, which died of rabies on the seventeenth day, January 11th, 1897, after having been trephined and subdurally injected from medulla oblongata of boy Eppers, who died of rabies on December 26th, 1896. The animals died on the thirteenth, fifteenth, fourteenth, and sixteenth days respectively.

Comments and Conclusions.—If one hundred children had been bitten by this same dog in an identical manner, *i.e.*, severe and numerous bites on the bare head and neck, how many would have likewise perished? A healthy rationality will admit the probability of eighty per cent., ninety per cent., even one hundred per cent. of deaths. These cases entirely corroborate all that is claimed by statistics on this point. That is, the mortality of bites of this description is eighty per cent., ninety per cent., even one hundred per cent., when not treated by the Pasteur method. But all these were treated by this method with a result as disastrous as if they had not been treated at all. It cannot be claimed that they were not timely treated. All were under treatment within about three days after having been bitten. Greater celerity than this is only very exceptionally attainable. Pasteur institutes cannot be located within three days' journey of everywhere. The only possible explanation is that some factor difficult of appreciation caused an unusually brief incubation and speedy onset of the disease. For the completion of immunization fifteen days after the termination of treatment are required. In these cases the disease outran the remedy. If fifteen to twenty days are required for completion of the treatment and fifteen days more for the completion of the immunization, then all cases which develop the disease in thirty-five days are not amenable to treatment. The stage of incubation in six per cent. is between three and eighteen days; in sixty per cent. it is between eighteen and sixty-four days. Granting the accuracy of these statistics from Bollinger' it may be assumed that thirty-five per cent. of children at and below eighteen years of age, suffering from multiple and severe and non-cauterized bites on the head

and face (bare), will fail to be benefited by the Pasteur treatment; sixty-five cases in one hundred escape when treated. Granting that twenty in one hundred would escape if not treated, then forty-five in one hundred are saved by the treatment. The foregoing remarks assume that there has been no defect in the administration of the prophylaxis. The Pasteur Institute, Paris, calls attention to the time limit, but does not plead this statute of limitation. It shows that all the deaths during treatment and at any time thereafter, from bites of the head and face, form only about six per cent. But this showing includes all ages, children and adults, and all bites, severe and slight, single and multiple. This is as inexact as the assertion attributed to John Hunter, that not more than five per cent. of all persons bitten by rabid dogs develop rabies. This may be true of slight bites through clothing, but it is entirely incorrect as regards severe multiple bites on bare parts, especially the face and neck. There are those who assert that mad-dog bites are very rare, and but very few of the few bitten develop the disease. But when they wish to impugn the Pasteur treatment they cite the present cases, asserting that fifty per cent. of the entire number bitten died of the disease, and one hundred per cent. of those bitten on the bare face and neck died. No sufficient number was bitten from which to calculate percentage. They "blow hot and blow cold in the same breath," and mean nothing unless they covertly claim that the treatment produced the disease. The virus of ordinary rabies, that of the mad dog at large, the street dog, *rage de rue*, when subdurally injected into rabbits, never produces the disease before the twelfth day; rarely before the fourteenth day. On the contrary, the virus of the laboratory, the virus of the rabbit at and beyond the fiftieth remove, when subdurally injected into other rabbits, produces rabies in seven or eight days. In the cases under consideration, the virus of the medulla oblongata of the boys produced rabies in the rabbit after about the same incubation as did the virus of the medulla oblongata of the street dog in question. The disease did not in any of the rabbits develop before the fourteenth day. Had the virus which gave these boys rabies been that of the laboratory, that which was used in the treatment, then the rabbits which were injected subdurally from the medulla oblongata of those rabbits which had been injected subdurally from the medulla oblongata of the boys would have developed rabies on about the seventh or eighth day. But it was demonstrated that on the ninth day after injection the medulla oblongata was not even virulent. The use of a second series of rabbits is necessary for two purposes: First, when the virus is passed from one species to another the incubative stage is variable in the first passage. In these cases—the virus from the medulla oblongata of the boys in-

jected subdurally into rabbits—the first rabbits might manifest the disease at some irregular period, probably a longer interval than its real incubative stage. But when the virus is passed from the medulla oblongata of these rabbits by subdural injection into other rabbits, then these other rabbits exhibit the disease after the stage of incubation normal to the virus. The normal incubative stage of the street virus is about fifteen days. The normal incubative stage of the virus of the laboratory which is used in the treatment is about seven days. Secondly, the other purpose necessitating the use of a second series of rabbits is to exclude the effect of traumatism on the nervous system. Very rarely a case occurs after trephining, even when the virus of rabies is not used, in which after a like incubative stage the rabbit develops a disease and dies with symptoms like those of rabies. That this disease and rabies are not identical is proven by the fact that this disease cannot be given from these rabbits to a second series of rabbits by trephining and subdural injection of their medulla oblongata; still less can it be so propagated indefinitely, as is the case in rabies, which is a specific infectious neurosis. The other disease is a traumatic inflammation or degeneration. Subdural injections into guinea-pigs or rabbits of emulsion of medulla oblongata from dogs suspected to have had rabies is part of the regular routine work of institutions practising the Pasteur method. Not infrequently the dogs are thus demonstrated not to have had rabies. Patients have been treated and the dog has been subsequently proven not to have had rabies. If a dog under suspicious circumstances bites persons and is at once killed, it is prudent to give these persons the benefit of the doubt and treat them. They cannot safely delay until the termination of an experiment which lasts over fifteen days.

Daily throughout the world institutions administering the Pasteur treatment demonstrate that rabies is a specific infectious (contagious) neurosis, and that no other disease is capable of producing identical symptoms.

In this necessarily discursive manner, the cause of rabies is shown to be something, some virus, some organism that has been communicated from one being to another. The mode of communication is by contact, and the vehicle, most frequently, is saliva. The contact, the conveyance, is usually by the bite of a rabid animal. It is well ascertained that the saliva of a dog may be virulent three days before the manifestation of rabic symptoms. "In the rabbit experimentally inoculated (subdurally) the saliva is virulent on and after the sixth day, the virus inoculated being a fixed virus (two hundred and thirty-seventh passage)." The first nerve symptom, incoördination, slight swaying, especially of the head and neck, from side to side when

disturbed, indicates in the rabbit the incipiency of nerve disorder, and the virulence of the saliva seems to be simultaneous. It has been shown that in subdural inoculation of rabbits with the unfixed virus the medulla oblongata is not virulent on the ninth day, but the condition of the saliva at this period has not been ascertained. "A dog inoculated in the anterior chamber of the eye had the rabic temperature rise eleven days thereafter, being 39.3° C.; previously it had been 38° C. and 38.8° C. Saliva at this period injected into the muscles of the neck of a guinea-pig caused it to develop rabies in fifteen days" (Roux et Nocard). There is obvious danger that abraded surfaces or wounds received in handling, experimentally or otherwise, rabid animals may become inoculated. That it is rare is no proof that it is improbable. If occupation brought human beings into the same association with rabies as with glanders, its transmission would be as frequent and as undoubted in the one as in the other.

Mode of Conveyance of Rabies.—The conveyance of the disease by parasites, fleas, lice, and other pests, from the dog, though not demonstrated is not incomprehensible as a possibility. Youatt cites a case in which a man untied a knot in a rope with his teeth and died of rabies, the rope having been used to confine a rabid dog; also another case in which a seamstress had her dress torn by a rabid dog; in repairing it she passed the seam, to flatten it, between her lips; she died of rabies. These cases almost overtax credence. To the class of literature designated as "fairy tales" the following cases belong. Van Swieten "reports that an old woman died with all the symptoms of rabies after a wound inflicted on her by an irate cock. He conjectures that the cock had been bitten by a rabid fox. If the disease were spontaneously generated in the cock, it is surprising it does not occur more frequently in England, where this irascible bird is trained to fight." The same authority asserts that "a young man died of rabies after having bitten his own finger in a fit of passion." Malpighi "declares that his own mother died of rabies a few days after having been bitten by an epileptic." Cases of spontaneous origination of rabies in man have been reported by Barthez and Gintrac, but Velpeau remarked that there was in these cases no sufficient evidence of the absence of contagion. Some portions of the body, denuded of epidermis, need only be in contact with the virus of rabies. Trousseau, who quotes these cases, remarks that "rabies in the human subject is always the result of inoculation with the virus of rabies." The present-time opinion almost unanimously regards this disease as never now originating *de novo*, any more than does glanders or smallpox. The communication of rabies in coitus is a far more remote possibility than is that of tuberculosis or carcinoma. Is the origin

of the disease ever congenital? "A cow with hydrophobia (rabies) gave birth to a calf, which developed rabies, although another cow had been substituted for it to suck from." A rabid cow has to my knowledge furiously attacked its own calf; herein is a source of fallacy. Excellent authority has demonstrated by subdural inoculation of the medulla oblongata of the fœtus of rabid rabbits that rabies existed in them; fallacy in this observation is reduced to a minimum. Milk of rabid animals has thus also been proven virulent, and it may be the vehicle for the transmission of rabies; but that the disease very rarely is so transmitted is the observation of the present writer and also of Perroncito and Carita.[1] The writer on several occasions has not been able to produce rabies by subdural inoculation from newly born offspring of rabbits with advanced rabies. "The milk and flesh of rabid animals—dogs, sheep, and cattle—may as a rule be consumed by man and animals without any ill effect. Gohier alone states that he has seen hydrophobia produced in a dog by eating the flesh of a dog dead of this disease, also by eating the flesh of rabid sheep. Hertwig made many experiments with negative results. Saliva and mucus from the mouth of rabid dogs were introduced into the stomach and throat of other animals, and they were fed with bread and meat smeared with rabic saliva, also placed in stalls with dogs which had recently died of this disease, given the same straw, food, washbasins, and chains, all without result." The disease cannot be taken through an intact mucous membrane, protected by its epithelium. Admitting that the risk is slight, still no risk should be run. Admitting, which is not absolutely certain, that an unabraded mucous membrane prevents the entrance of this virus, slight abrasions are easily made and readily escape observation. Youatt held that the virus was absorbed by the mucosa.

Rabid animals are thoroughly diseased animals. Their flesh should not be used; nor should their skins be used, though they are less dangerous than those of animals afflicted with anthrax.

Attenuation of Virus.—"The virus of rabies can be weakened, attenuated; when it is passed from the dog to the monkey and from monkey to monkey it grows weaker at each passage. After the virulence has been thus diminished by several passages through monkeys, if the virus be carried back to the dog, the rabbit, or the guinea-pig, it still remains attenuated. In other words the virulence does not go back to the degree it had in the dog. A small number of passages from monkey to monkey suffice to so attenuate the virus that it does not give rabies when hypodermically injected. Intracranial inoculation itself, the never-failing means of communicating rabies, may now remain without effect, while, however, creating a refractory state in

favor of the inoculated animal" (Suzor). "The virus of rabies in the lymph sac of the frog becomes attenuated in fifteen days when it becomes a sufficiently strong vaccine for a dog, but not for a rabbit. A mixture of the blood of immune dogs with rabic virus sterilizes the latter in six hours. The frog does not contract rabies, though its migratory cells are to be seen in the nervous substance (gray matter) a few days after the introduction of the rabic medulla into the dorsal lymph sac. Pasteur preserves cords by dry air (suspended over caustic potash). It is now known that heat plays the most important part in these experiments, and it may act by favoring oxidation" (Babes, Gerchez, and Protopopoff).

The virus of rabies subdurally inoculated into the hen has a long incubation, and at the death of the hen its medulla oblongata will be found to be sterile. It does not give rise to rabies when it is inoculated subdurally into rabbits. The temperature of the hen in the cloaca is 108° F., at which temperature the virus of rabies can be sterilized in vitro.

Character and Seat of Bites in Relation to Causation.—In the causation of rabies by bites much depends upon the seat, number of bites, severity, and whether the part be naked or clothed or covered with thick hair. The neck is selected for experimental hypodermic injections of rabic virus, because these injections are more frequently successful in this region than elsewhere. The injections are made deeply into the neck muscles and it is suggested that the virus should come into contact with the cervical nerves at their exit from the spinal column, as in this way it will more rapidly and surely reach the anterior columns of the cord.

Numerous, extensive, deep bites on the face and neck are very dangerous. They are estimated to result fatally in 80 to 90 per cent.; on the hands, 63 to 67 per cent.; on the body, 31 to 63 per cent., the latter in numerous wounds; on the upper extremities (arms), 20 to 30 per cent.; lower extremities (legs), 21 to 28 per cent. The general percentage is stated at from 55 to 47. If the wound be cauterized properly and timely, 33 per cent. of those bitten take rabies; if not cauterized, 83 per cent. Age exerts no appreciable influence on deaths from rabies. Under twenty years the mortality is 31 per cent.; over twenty, the percentage rapidly goes up to 62.

The following table is from Bollinger:

12	between	3 and	5 years.	49	between	20 and 40 years.	
27	"	5 "	10 "	36	"	40 "	60 "
62	"	10 "	20 "	9	over	60 years.	

Wide discrepancies in estimates result from difficulty in arranging,

in sorting factors. It may be assumed that a bite cannot put the virus more surely or in greater quantity into the body than can a hypodermic injection. If it be assumed further that the guinea-pig is of average susceptibility, then this animal treated subcutaneously in the trunk with a fixed virus gives from sixteen to eighteen per cent.; when the injection is made deeply into the muscles of the neck the percentage is much greater. The percentage of fifty in deep and multiple wounds of the face and neck is by no means an overestimate. "In what manner or by what course the poison penetrates the body from the seat of the wound is absolutely unknown." This assertion by Bollinger is almost twenty-five years old and has received some little elucidation more recently. Any condition that favors contact of the virus with the nerves facilitates the production of the disease, because "the lymph channels of the nerves are more directly in communication with the lymph spaces in the cerebrospinal canal than are other lymph channels," yet the cerebrospinal fluid is not always virulent. It is an observation of Pasteur that sometimes this fluid, though perfectly limpid, produces the disease, and sometimes it fails to do so even when turbid. The blood is rarely virulent. Pasteur produced rabies only once from the blood. He called attention to the certainty of infection by intravenous injection. "The nerves are not the sole channels of propagation of the virus from the periphery or surface to the centre." "We (Pasteur says) have on several different occasions inoculated the virus into one of the veins of the ear and then immediately after cut off that organ with the thermocautery between the point of inoculation and the head. Nevertheless rabies showed itself in every instance, although the thermocautery does not produce an open wound, the whole of the cut surface being burned." Though the blood-vessels themselves are diseased, the blood itself exhibits no change and is rarely inoculable. The virus may preferably (chemotaxis) go by the way of the lymph route. The coats of these blood-vessels may be diseased from the lymph channels without and not from the blood within. Perhaps the virus avoids the serum, finds it repellant. Put into the circulation it speedily makes its way out, indicating that blood serum is not a desirable culture medium, either naturally or artificially. That the blood does suffer when in contact with this toxin will be adverted to more in detail in the section relating to pathology.

"If in the dog the spinal cord be cut across, and afterwards one of the nerves of the hind foot be inoculated, the cord below the cut will produce rabies when inoculated, but the part of the cord above the section will be found not to be virulent. The same holds good when a similar experiment is made by injecting a nerve of a fore limb. When

the disease develops slowly as the result of a bite of a limb on one side of the body, the peripheral nerves on the opposite side may also contain the virus" (Woodhead). These experiments indicate that nerve matter is a desirable culture medium, naturally and perhaps artificially, with brain and lymph in combination. The deduction from this is that a part abounding in nerves and lymphatics, and somewhat close to the spinal origin of the former, is a danger point; and this is equally strongly substantiated clinically. The filtrate through porcelain, injected experimentally in the dog, causes paralytic symptoms. The entire pathological phenomena are typical of intoxication produced by material loosely designated as toxins. The salivary glands, especially the parotid, and also the lacrymal secretion (which may perhaps cause the ocular inflammation, keratitis, etc.), the mammary secretion, the pancreas, and the suprarenal bodies are virulent. Pasteur demonstrated the presence of the rabic virus in the lumbar swelling of the spinal cord occasionally before it was present in the medulla oblongata. The disease has been produced by pieces of the pneumogastric nerve near its cranial origin and distant therefrom; also by pieces of the sciatic and submaxillary nerves. The presence of the virus in the peripheral nerve distribution explains in man the strange symptom aerophobia, as does the involvement of the respiratory centre explain the asphyxia which is not well designated as hydrophobia.

Fanciful etiological factors are season, temperature, want of freedom and food, age, sex, race, and restrained sexual indulgence. The best observers hold that these act neither as direct nor as predisposing causes. Fanciful scepticism is adverted to as follows by Boulanger: "The denial of the existence of hydrophobia as a specific disease lately by Mascha and Lovinser (1865) has not even the merit of novelty, for the existence of hydrophobia as a disease *sui generis* as well as the existence of a specific virus was denied in France by Bosquillon (1802). According to their views the symptoms are ascribed to fright or to the local injury. Girard and J. Simon (1819) regarded it as an imaginary disease. R. White (1826) regarded hydrophobia as nothing more than an ordinary inflammation of the œsophagus, the stomach, and muscles of respiration. He denied not only its specific character but also its infectiousness. He inoculated several cats, rabbits, and other animals, and finally himself from two rabid dogs, all without result. It is hardly necessary to add that these negative results, as compared with numerous positive results following inoculation and with simple clinical experience, are entitled to no weight, and are valuable at most only as illustrations of foolhardiness indulged in with impunity." "The spontaneous origination of rabies is as

incredible as that of smallpox or as spontaneous generation in the abstract. Virchow states that the doctrine of the spontaneous origin of rabies contributed most of all causes to involve in doubt the specific character of the disease. He regards the action of the poison of rabies as comparable to that of yeast, fresh particles constantly being conveyed into the blood from the seat of the inoculation, producing through the medium of the circulation its specific effect upon the nervous system. The resemblance to alcoholic intoxication and to certain forms of mental affection is unmistakable, the poison in each case producing its effects upon the centres of the medulla oblongata and cerebral hemispheres."

The cause of rabies is an infectious (contagious) virus capable of indefinite propagation when inoculated through wounds and abrasions and also through unabraded mucous surfaces. Age does not of itself markedly affect it, nor does putrefaction in a reasonable length of time. Moderately high temperatures acting in experiment tubes attenuate and destroy its virulence.

Virus Attenuated by Heat.—It has been previously stated that cords in a condition of early putrefaction kill rabbits and other animals by septicæmia, and that the organism is that of rabbit septicæmia; but when putrefaction is advanced, the cord, if a rabic one, causes rabies. "Rabic cords in an incubator for eight days at temperatures of 30°, 35°, 40°, 45°, 50° C., when subdurally inoculated resulted as follows: 30° C. killed with rabies in about nine days; 35° C. in eleven and twelve days; 40° C. caused symptoms of rabies, but the rabbit did not die; 50° C. were not at all affected." At 86° F. the rabic cords were little if at all weakened; at 95° F. the incubation is markedly prolonged; at 104° F. the disease was mild and recoverable; at 122° F. the cords were sterilized. It is known that heating to 108° F. rapidly renders the rabic virus in tubes inert. Such is the experimental effect of heat on rabic virus outside the body. Rabic virus in a body having the temperature of the hen (108° F.) is sterilized, but too late to prevent the disease, though its incubation is prolonged. The late Dr. J. M. Byron, of New York (1888), from whom much of the above account is quoted, remarks that the rabbits inoculated with cords that had been exposed for eight days to 40° C. and 50° C. did not acquire immunity, but when subsequently inoculated developed rabies; these cords were not of the nature of vaccines. He adds: "These experiments in tubes prove nothing more than an attenuation of virus by temperature, and cannot indeed be very happily compared with what happens to the animal organization under the influence of a hot climate. They explain some things but not all. Experimentation in the way of submitting animals to conditions that resemble the

atmospheric phenomena, after having been inoculated with cords with the maximum of virulence, is the only way of resolving the problem." Dr. G. Ferris, in seeking the cause of death by rabies, was induced to try warming the animal, which in the paralytic stage becomes rapidly cold. By this means he succeeded in prolonging life one, two, and sometimes three days. The effect of natural high temperature on the rabic virus in the body of the hen (the temperature of which is 108° F.) is to render it sterile, inert, innocuous. The cloaca of the hen might be used for minor experimental purposes as a thermostat set at 108° F. The effect of artificial external heat on the rabic virus in the body will be considered in the section on therapeutics.

Preservation of Virus.—Rabic virus retains its virulence intact for several weeks in the encephalon and cord if the cadavers are preserved from putrefaction by keeping them at a temperature ranging from 0° to 12° C. (32° to 53° F.). The virus, enclosed pure in glass tubes sealed by the blowpipe, can be preserved for three weeks or one month even at summer heat. Dr. Byron suggested that a test tube be used with cotton soaked with glycerin and water at the bottom of which the cord rests; the open end of the tube is sealed by the blowpipe. Cords thus prepared can be safely transported. The following method I have used advantageously: Take a sterilized test tube containing glycerin agar, flame the cotton plug and perforate it with a red-hot needle; then thrust the cotton down nearly to the agar, and seal the open end. The agar will exhibit growths should the material (cord) become contaminated. Fluid culture media can of course be used if the tube is not upset. The virulence of rabic material is best maintained at a temperature of about 23° C.

Incubation.

The stage of incubation is of variable duration. In six per cent. of all cases between three and eighteen days, in sixty per cent. between eighteen and sixty-four days, in thirty-four per cent. this stage exceeds sixty days. While this period is seldom less than fourteen days it is frequently protracted from three to six months. There is an authentic case in which the duration of the period of incubation was eighteen months. But a duration of five, seven, ten, and twelve years should be obviously regarded as mythical. Fourteen days and five years have been given as extreme limits. Brouardel quotes the following statistics: Out of one hundred and seventy cases rabies showed itself in all within the first three months; in another set of ninety-seven cases it declared itself within the same period. He concludes that rabies supervenes oftenest in the course of the second month; rarely

after the third month; quite exceptionally after the sixth month. The more numerous the bites and the greater their gravity the earlier do the symptoms appear. They manifest themselves earlier also in children than in old people. I have known four children (boys), the eldest being sixteen years, the youngest eight years, all bitten by the same dog at or about the same time, to develop rabies within thirty-five days, notwithstanding treatment. These children were bitten on the face and neck, and not efficiently cauterized (efficient cauterization in multiple and deep wounds is impossible). "The dangerous period for children bitten on the head and face rarely lasts beyond the fourth or sixth week." This assertion would be more in accord with strict fact if the bites were qualified as multiple and severe. Of course a mere scratch or puncture may cause the disease, especially if a nerve be involved; but such wounds can be more radically dealt with, and they are less apt than multiple and severe wounds to lacerate nerve and lymph structures. The foregoing relates to rabies in the human body.

In the dog the duration of incubation is "less than two months in eighty per cent. of the cases; very seldom longer than six months. Youatt gave one case of eleven months." The longest period of latency in the dog is fixed at eight months; the shortest at six to eight days. The disease occurs within two months in eighty-three per cent., within three months in sixteen per cent., four months and later in one per cent. In other domestic animals the period of incubation varies from two to five, seven, or ten weeks, and in exceptional cases may be extended to nine or fifteen months. During the stage of incubation the persons bitten (so far as observed, for minute observation in man is difficult) exhibit no symptom. They themselves have often forgotten the occasion of the bite. Slight wounds readily heal. Bites of rabid animals, even after the application of strong caustics, are said to manifest a strong tendency to heal without granulation. Inflammatory reaction is generally slight and its pain moderate. Touching the scar is said to produce peculiar sensations—shuddering, feeling of anxiety, and sighing. It is necessary not to overrate the tingling, smarting, burning, drawing, and darting painful sensations which are common in all cicatrices; atmospheric changes, rheumatism, neuralgia, may beset any cicatrix, and not rarely those produced by caustics.

These remarks are restricted to the stage of incubation. The early symptoms, the prodromes, exhibit cicatricial signs more frequently in the lower animals, but they are present exceptionally in man. In animals there are experimentally observed in the period of incubation peculiarities of temperature and respiration; the former are easily

recognized and of ominous portent. Dr. G. Ferri (1889) claims to have observed in inoculated rabbits a period of acceleration of respiration sometimes on the fourth day after inoculation, more frequently on the fifth. He advances the theory that this indicates the arrival of the poison in the floor of the fourth ventricle, which becomes virulent between the middle of the fourth day and the commencement of the fifth day. He does not think that elevation of temperature produces the acceleration of respiration. The temperature in seventeen out of forty-seven animals rose after inoculation, thirteen on the second day, three at the beginning of the third day, one at the end of the first day; then the temperature fell below the point of elevation some tenths of a degree. Feeble variations continued for five days, during which period for the greater part of the time it rose. It attained a maximum in the majority of cases on the sixth day, fourteen times on the fifth day, thirty times on the sixth day, three times on the seventh day. From the time of the highest elevation it began to descend and continued to do so until the death of the animal. The relative maximum on the second day is not constant; the absolute maximum occurring on the sixth day is constant. The relative maximum is only .74 of a degree; the absolute maximum is 1.5 degrees. This may be called the rabic rise of temperature. We have seen it fail in only one case. If the accelerated respiration was caused by the elevation of temperature, the maximum of respiration ought to coincide with the maximum of temperature. Furthermore, the latter occurs on the sixth day while the former takes place on the fourth day. In some cases the abatement of the respiration has begun before the maximum elevation of temperature had been attained; consequently the respiratory acceleration does not appear to be dependent on the elevation of the temperature. In certain cases, however, it does appear as cause and effect, but in a general way one may say that the accelerated respiration occurs when the floor of the fourth ventricle becomes poisoned and is independent of the thermal phenomenon.

The saliva of the dog is virulent three to eight days before any sign of rabies appears; the saliva of the rabbit at the time of the temperature rise, on the sixth day. Marachetti's eruption beneath the tongue, knots, vesicles, swollen orifices of the submaxillary glands observed by him and by Drs. Magistel and Zanthos, may perhaps occur at times in various disorders, but are of no significance as indicating incubation of rabies. I know of no observations regarding temperature in human beings during this stage of rabies.

Rabies in Animals.

Dogs.—There are two varieties of rabies. One is popularly recognized and feared as a dog runs mad. There is another in which the dog does not run; it is in fact paralyzed and cannot. It seeks retirement, hides away in obscure places, in fence corners, cellars, and under steps. Fortunately the animal does not tend to bite. In the early part of this condition biting is difficult; in the latter part it is impossible. The jaw is in a condition of paresis, and from the open mouth drivels a virulent saliva. Sympathy for animals is a commendable trait; but in the case of sick or wounded animals it should be manifested with caution. A little dog run over by the street cars was picked up by a gentleman, who was bitten by it on the hand. From this wound rabies developed. A stray cur taken in by some children was fed by their father, who in stooping to feed it was bitten on the ear and died of rabies.

The typical mad dog exhibits three stages. In the first the dog is dull, depressed, fidgety, nervous, restless. In the second it is delirious, maniacal, furious. In the third stage it is imbecile, helpless, paralyzed. In the beginning of rabies there is an alteration in its usual behavior and disposition. In its conduct it evinces a variable disposition to those around it, being either more confiding and friendly than usual, or the opposite, irritable, morose, and easily enraged. An undemonstrative cross dog becomes friendly or even caressingly affectionate. An amiable dog becomes snappy and cross. There is a peculiar condition of hyperæsthesia at times; the animal crouches away from the touch and is easily frightened. There is moderate conjunctivitis, the eyes are red, sad looking, and distrustful. The attitude indicates suspicion and sickness. The appetite is disordered. The dog refuses food, except some choice bits, and the food is apt to escape from its mouth; it drops it. On the other hand it swallows all sorts of unfit things—hair, straw, dung, rags, earth, stones, bits of leather, and wood. It licks cold objects eagerly—stones, iron, and the noses of other dogs—and also its own urine. At times the sexual instinct appears to be excited, the animal constantly smelling and licking the genitals of other dogs. It is shy, uneasy, springs at the door, has spectral illusions, and obeys reluctantly. Its movements show signs of uncertainty, incoördination; there is weakness and tremulousness of the hind part of the body. It wanders about the house and yard, seemingly seeking a remedy for its discomfort. It may still obey its master, and in most cases spares those to whom it is attached; but if persistently disciplined it may lose its self-

control and bite. It may lick and gnaw its wounds and cause them to become inflamed. Sometimes there is excessive itching. The eye is frequently closed for several seconds; there is defluxion from the nares, a tendency to choke, difficulty in swallowing, and a disposition to vomit.

The voice—and this is an important sign—even at this early period is altered, hoarse and muffled in the bark, which is rather infrequent and difficult to evoke. It is, according to Bouley, quite peculiar, and once heard is not forgotten. "Instead of bursting out with its usual sonorousness and being made up of a succession of notes equal in duration and in intensity, it is hoarse, veiled, lower in tone, and after a first full-mouthed bark there follows immediately a succession of five, six, or eight howls coming far back from the throat, and during which the jaws are never completely closed, as they are ordinarily after each bark. It is not unlike the voice of a dog chasing a hare; it is something intermediate between a bark and a howl made up of the two with something added, stronger and sinister" (Suzor). In some cases the dog is voiceless.

As a rule the stages gradually pass into one another. Sometimes there is a sudden outburst. The symptoms of this first stage may be very insignificant; nor are they uniformly present. And for this reason the greatest risk is incurred by man at this stage. Many of these symptoms are of short duration and, moreover, are present in other diseases; therefore their diagnostic import is slight. The dull, voiceless dog crouches in the dark and quiet, trying to sleep, but its slumbers are broken by dreams, hallucinations, and delusions, which also characterize its waking hours. "Seeking rest and finding none," it gets up and walks about. In some cases there is an absence of this restless agitation; it is sleepy and pays no attention to what is going on around. If disturbed it growls but shows no inclination to stir. This condition may usher in the paralytic variety, but it occasionally and for a time is present in the typical rabies. There seems to be a displacement of special symptoms, and indications exist of that which subsequently becomes very pronounced. The slight paralysis, paresis of the first stage, indicates the complete condition of the third; transient outbreaks of violence presage the furor of the second stage. Slight alteration of voice precedes its marked change and final extinction; excitability increases. In a room the dog runs about persistently, noses under the furniture, tears the curtains and carpets, bounds at the wall, jumps and snaps as though catching flies. It sees things which are not, and hears sounds that have no outward source. All this, says Youatt, may be dispelled by its master's voice. The dreadful objects vanish and it creeps to its master with the expression

of its peculiar attachment. Now follows an interval of calm. It slowly closes its eyes. Its fore legs give way and it seems about to drop. Suddenly it gets up again. Fresh phantoms rise before it. It looks about with a savage expression and rushes as far as its chain allows against an imaginary enemy.

It is thirsty, laps fluid eagerly but cannot swallow it; but in some cases it can swallow solids, and this it does without discrimination, so that foreign and unusual substances in a dog's stomach arouse suspicion of rabies. It bites and tears rough substances, lacerating its mouth so that blood in the trachea, œsophagus, and stomach is not unusual. At first for a short time the appetite may be increased, but soon it is lost. But the dog may eat or at least swallow or gulp down food and other things within reach. The popular idea is apt to be rash and sweeping in generalization. If a dog can and does eat it cannot be mad, may be a rule, but it has exceptions. A patient assured me that a dog which bit him, ate naturally all the time. I know that it swallowed meat put in its box, for I saw the meat put in, and after observing it all the time I had it shot and found no meat in the box. It took the muzzle of the pistol, which had been thrust through a knot, between its teeth; the discharge tore its medulla oblongata to pieces. The dog at times will respect its master and recognize his voice, but not always at all times. A gentleman recounts the circumstances under which he was bitten: "My dog had abandoned its home, but returned. I called it; it then rushed upon and bit me. If I had not thus attracted its attention I do not think I should have been bitten." Another idea with an element of truth is that a mad dog usually runs straight, will not deviate from its course. This it may do when amaurotic, almost blind, pupils widely dilated, weak, and tottering. It may have no inclination to go aside. But when it will and when it will not is a factor impossible to determine practically.

The foregoing is a composite picture of the first stage of furious rabies. Very rarely does the one case present all the features, and very rarely also some one case may present none of them. "The animal remains tame and unaggressive to the end, but as a rule in the second stage it is in a state of delirious rage, about which there can be no mistake as to its significance. If chained in a cage it bites and tears at everything thrown at it. It attacks furiously all animals that come within its reach, later on man also, and more rarely its own master." It seems to have lost the sense of pain or the expression of it. It breaks out its teeth and tears its body. If now it can break away, and it makes strenuous efforts to do so, it runs amuck biting many other animals, and some of these in their turn

developing rabies propagate it endemically. It is no unusual experience in institutions for the treatment of rabies to have several patients from about the same district bitten at distant intervals of time. The advice to kill all animals bitten is sound, but in rural districts it is impossible to know all the animals that have been bitten. The familiar picture of the tail drooping between the legs, the open mouth, the dripping saliva, the sideways gait, the stagger, is that of the beginning of the end of the third stage. Before further adverting to this stage it is important to note that a mad dog, fighting and biting furiously, *rarely or never barks*, which other dogs in fighting do incessantly.

Viewed from a distance the wandering mad dog presents no peculiarity of gait; its tail is held high and wagging, there is no dribbling of foam so long as it can swallow. "Its course is sometimes straight forward, sometimes in diverse directions or in circles." No especial dread of water is manifest, nor is there aversion to air, to light, or, except in rare instances, to the glare of the sun. The fæcal and urinary excretion is scanty. As the dog eats but little there is not usually any bowel obstruction. Occasionally the large gut is filled with dirt and hair. Emaciation is rapid, caused by excessive waste and excretion, the eyes become sunken, the coat rough, and the body thin. The mucous membrane of the mouth is but slightly moistened and is often parched and of a dirty livid color. A discharge of saliva and foam from the mouth is scarcely ever seen. The respiration may be hurried, but is usually but slightly affected. The pulse is slightly accelerated and often irregular.

The third, the paralytic stage, develops directly from the previous stage, the paroxysms becoming weaker and less distinctly separated from the remissions. The maniacal rabid dog, like the human maniac, after a longer or shorter duration of furor has longer or shorter periods of exhausted quiescence. Increasing exhaustion, increasing paralysis, especially of the hind legs, ensue. The gait becomes uncertain and staggering; the dog can scarcely stand and totters from side to side. Often it lies curled up as if attempting to sleep, raising itself on its fore legs only when irritated. It may still attempt to bite or at least snap; the voice is hoarse, there is dyspnœa, and a small, thready pulse. At times partial or complete convulsions occur. Death usually takes place on the fifth or sixth day; it is rarely prolonged to the seventh or eighth and never beyond the tenth day.

Paralytic Rabies.—Inoculation experiments from this form of the disease (dumb madness, sullen rabies) often reproduce the disease in its furious form and *vice versa*, showing that the two forms are only varieties, though very different, of the same disease. This form of rabies exhibits itself in about fifteen or twenty per cent. of all cases.

Formerly this form was supposed to be the first stage of the disease and the rabid form the second stage. Now it is regarded as the immediate passage of the first stage into the third stage, the second stage having been omitted. Experimentally in young dogs the disease may begin and end suddenly and abruptly in the second stage.

On June 14th, 1897, a bitch was trephined and inoculated subdurally from the medulla oblongata of a rabbit dead of rabies from subdural inoculation of a fixed virus; one hundred and twenty removes. On June 23d, at 8 A.M., at which hour the previous evening there was no grossly apparent disease, the animal was running about the cage, biting at its sides and at the vessels in the cage, and butting its head against the walls. Its bark was hoarse, howling, squeaking. It had three tetanic convulsions and died at 10 A.M. the same day.

Post-mortem Examination.—Integument of scalp contused by butting the walls of the cage. Lungs ooze serum freely; kidneys hyperæmic; bladder empty; stomach contains sawdust and hair.

January 15th, 1898: Black and tan cur, young, not fully grown; weight, ten pounds. Trephined and subdurally injected with emulsion, in sterilized water, of medulla oblongata of rabbit which died of rabies from subdural inoculation of fixed virus; one hundred and thirty-eight removes.

January 24th, 7:30 A.M.: Biting basin and growling. 8:30 A.M.: Barking, apparently naturally. Biting sides of cage, jumping and falling about. Broke its teeth, seized its hind leg between its teeth, held it, chewing on it and biting it. 1 P.M.: Same dog exhausted, and now made no attempt to bite a bitch put in cage with it. Just before death it barked, apparently naturally; convulsed, it died at 1:30 P.M.

At 4 P.M. the previous day, the dog was gentle and answered when called, jumping up on the sides of the cage. Without doubt the saliva was at this time virulent. Had this dog bitten some one and passed from under observation, and the bitten individual subsequently died of rabies, a biassed mind would see a case of rabies from bite of dog that had it *not*. A fact relative to alteration of voice is noteworthy. The hoarse tone of voice, the peculiar laryngeal vocalization may disappear at irregular intervals and return. I have observed this in a human being with rabies. Though generally his utterance was laryngeal for a few moments, a few sentences were uttered distinctly, showing that at this time the nerve disorder was one of incoördination, paresis rather than at this period of complete paralysis.

The medulla oblongata of this dog was injected subdurally into a small young black and tan cur, weighing nine pounds. This was done on January 24th. On February 1st, this dog suddenly de-

veloped furious rabies. The evening before it was gentle and timid. It furiously attacked a dog put in the cage with it, fighting and all the while not barking. The bitten dog has not at this date, June 9th, 1898, shown any sign of rabies. The rabid dog was observed to have the disease about 7 A.M., and died at noon on the same day exhausted. When fighting with the other dog it would become exhausted and lie down panting, and after a time get up and renew the attack. These cases strikingly contrast with that of an immense, previously ferocious bulldog; which being experimentally rabid could not be forced to bite another dog, and Pasteur was compelled to take the saliva from its mouth. He remarks that it is well known that a bitten dog, if it takes the disease, shows in the majority of cases furious rabies with a propensity to bite and possessing the special rabid voice.

In the habitual run of our experiments, when we inoculate the rabies virus into a vein or the subcutaneous cellular tissue, we more often give rise to the dumb or paralytic form of rabies, voiceless and tame. By intracranial inoculation, on the other hand, the rule is that furious madness is produced. We have also ascertained that it is possible to give rise to furious madness by intravenous or subcutaneous inoculation, provided that very small quantities only of the virus be used. The smaller the quantity of virus or diseased material used in the entire venous or hypodermic inoculation the more certainly is the furious form of rabies reproduced. By the inoculation of small quantities of virus the duration of incubation is increased, and the same virus, if diluted beyond a certain limit, which is not very far, remains without effect when inoculated. Let it be carefully noted that a fixed virus inoculated in very small quantities may produce a very prolonged stage of incubation in the first passage, but a second passage, with the usual quantity, exhibits the incubative period of a fixed virus.

In paralytic rabies the disease runs a shorter course. The symptoms of cerebral irritation are slight in degree, the animals are less lively and active, appearing silent, quiet, and depressed (even in human beings with this form of rabies silent gloom and unnatural passivity, morbid inactivity, are marked characteristics). Excitement, the propensity to stray or to bite is less frequent. There is no aversion for fluids. The voice is a howl with no admixture of bark, and soon is lost altogether. The mouth is constantly open, owing to paralysis of the lower jaw; the eyes are without expression and constantly fixed in the same direction. The predominant symptoms are muscular weakness and cerebral depression. The animal is constantly lying down or sleepy; it has neither the will nor the power to bite. Everything taken into the mouth falls out again. There is

the genuine frothing saliva with mucus flowing from the open mouth. We see absence of defecation, no appetite, rapid emaciation, and death much more quickly than in the furious variety, taking place within two or three days.

The great majority of cases of canine rabies end fatally; a few exceptional cases are, however, on record in which the disease spontaneously or under the influence of treatment gradually disappeared. Submersion in cold water until asphyxia is nearly complete; the so-called sailors' cure; the bakers' hot-oven cure; the excision of the sublingual vesicles, calomel, bleeding, enemata, broom top, and other vaunted remedies are unworthy of scientific credence. That dogs and other animals have recovered after the manifestation of the very early symptoms there can be no doubt, and they may thereby acquire immunity. That in man, under similar circumstances, the same might take place is a possible occurrence of which there has been no rigorous scientific demonstration.

Rabbits.—The symptoms of this disease in the rabbit are interesting in themselves, and additionally so because this animal is usually selected for the demonstration and production of rabies, and its spinal cord is used in prophylaxis. The rabbit is inoculated by trephining and the subdural injection of rabic medulla oblongata rubbed up in bouillon or sterilized water. A piece of medulla from the floor of the fourth ventricle, of about 4 c.mm., is rubbed up in about 10 c.c. of sterilized menstruum, and of this three or four minims are injected beneath the dura mater, or small pieces (about 1 c.mm.) may be introduced through small slits in the dura and gently pressed against the brain and withdrawn, or they may be allowed to remain. If the virus be not fixed, if it be from some animal ordinarily rabid, the first signs of the disease manifest themselves between the twelfth and twentieth day, usually on the fifteenth day. With the fixed virus the first manifest sign appears on the seventh day, that is, after six days. This sign is elicited by pushing the rabbit. A sudden, quick push sideways, alongside the thorax, causes the rabbit, in regaining its equilibrium to oscillate from side to side; especially is this observable in the head and neck. The eyes are unusually glistening and the ears are often held erect. In some cases there is marked gritting of the teeth and continuous chewing movement of the lips. The incoördination just referred to rapidly increases; in twelve hours the rabbit falls sideways if caused to run, or tumbles on to his back, kicking and struggling ineffectually to get on his feet. There is often a grotesque pose, the head is thrown backwards or to one or other side and shaken; the limbs are projected before or behind or sprawled out laterally; the body may be curved sideways or bent backwards in marked opistho-

tonos, in which position after death it becomes fixed. This incoördination eventuates in complete paralysis, the rabbit lying helpless on its side. But in this first stage there is no ordinary paralysis; the animal held up by the skin of the back kicks vigorously. There may be slight convulsions, or the tremor always present may amount to a convulsive movement or the convulsion may be very violent. But with all this muscular exertion the low temperature of this stage is maintained; the thermometer introduced its entire length up the rectum indicates no rise of temperature. Generally the incoördinate stage is very marked; sometimes it is very slightly if at all present in these cases; the paralytic element predominates from the first. The animal is loath to move, is stiff, and drags itself along with difficulty. The whole body is depressed downwards, the belly too close to the ground. The muscles of the scapula and pelvis seem paralyzed and allow the body to settle downwards. The animal tends to be more quiet in this form than in the first.

Furious rabies cannot be predicated of the rabbit, but it has its semblance in an excited form. Occasionally the rabbit does not exhibit the usual incoördination or the rarer paralytic form. Let out of its cage into the room it runs about excitedly. After running for a time forwards, it runs backwards several steps; it stops still and jumps upwards, thrusts its head in a corner and paws at the floor; and this pawing it repeats energetically if disturbed. If a stick be pushed at its mouth it makes some forward movement of its head as though about to bite, but it is doubtful. A rabbit can perhaps be taught to bite a person, but it is not its natural inclination. I have known an employee to be bitten because he, placing his hand beneath the rabbit's mouth, moved it (his hand) from side to side on the floor of the box, spreading the sawdust; this manœuvre is a risky one. The finger was somewhat badly cut, and the attendant was treated because the rabbit developed rabies in twenty-four hours after the bite. In the excited form paralysis ensues, but it comes on late as a last stage; the incoördinate stage has been replaced by the excited stage. This stage of incoördination, so emphasized in the rabbit, finds expression in other animals in their tendency to fall down. Their legs give way under them. The rabbit not infrequently tears open the operative wound and paws it apart, because of some disagreeable sensation. There is a mucopurulent discharge from the conjunctiva. The cornea sometimes becomes opaque. The stools are pultaceous; not balled as normally. Before the onset of the nervous symptoms there is a rise of temperature, irregularly coming and going when the disease is a result of unfixed virus. With the fixed virus the temperature elevation immediately precedes

the nervous symptoms. It soon falls and continues to drop until death.

The domestic tame rabbit is used for experimental purposes; the wild rabbit cannot be handled and dies in captivity, injuring itself by violent impact with the cage. The wild rabbit bites persons when it is well, and would also do so if sick with rabies. Why the domestic rabbit with rabies does not bite man it is not easy to explain. To say that biting is not a natural mode of offence and defence with a tame rabbit is to mistake a fact. The buck rabbits are very fierce fighters, biting each other's bodies like dogs and tearing with their teeth each other's ears. They also bite and tear out the testicles.

Excited rabies, according to Pasteur, is more apt to supervene in first passages—that is, from one species to another, but it is not absolutely absent in inoculation with fixed virus. Pasteur believed that an animal is more apt to escape when a very large amount of emulsion is injected than when the dose is the usual medium amount, five minims; he assumed that a large amount of antitoxin is also injected. Rabbits inoculated should be kept under observation at least ninety days, because it is known that rabies may develop after such an interval of time. Dr. Wesbrook (University of Minnesota) has informed me of an interesting series of this nature.

Horses.—As usually observed in the horse rabies is of a violent character; not that the quieter forms do not exist in this animal, but they escape observation or are ascribed to other causes. The horse, at the beginning of the attack, is excited and subject to illusions. Excessive fright speedily ensues with tendency to bite, neighing and gnashing of teeth, sexual excitement, and loss of appetite. The specific paroxysms are very severe; the animal begins to kick, strike, and bite the objects about it, or held towards it. It often wounds itself, tearing off with its teeth portions of flesh of the fore legs and flanks. It will also seize other animals. It rubs the nose and mouth and makes peculiar motions with them. Respiration is accelerated. Weakness and paralysis of the hind parts take place. Death generally results in four or six days.

A mare, weight eleven hundred pounds, aged twenty years, was bitten by a supposed rabid dog, October 11th, 1893, was taken sick November 1st, and died November 2d. The mare was stiff and would fall down. Had tonic and clonic convulsions with head retracted. Saliva was running from the mouth. The mare bit the stall and a man, but she could not eat, could not swallow. Fæces and urine were involuntarily passed. Post-mortem examination showed a rupture of the serratus magnus and diaphragm, supposedly from spasm. The medulla oblongata seemed softened, and there were numerous

small hemorrhages into its substance. The dog that bit this horse had changed voice, snapped at chairs and bushes, and could not drink. Tongue black and "drawn up to a chip" in its mouth. From the medulla oblongata of this horse rabbits were trephined and inoculated subdurally; sixty rabbits developed rabies from this medulla, which has been before referred to.

The following article from a lay journal * graphically describes the disease: "Mr. Scott Mackey's dog has gone mad and bitten a horse and cow. The horse has since gone mad; went mad just four weeks from the time she was bitten. While hauling fodder it was noticed that the horse was very irritable and in other ways acted rather strangely. After dinner Mr. Mackey saw that she had eaten none of her food, and for fear she was going mad he placed her in an empty pen of his hay barn. The next morning a man looked through a crack of the barn at her, and with her mouth open she plunged towards him. Her colt was lying between her and the crack and she caught it by the top of the neck. All day she was pawing, neighing, and shivering as with cold (tremor?); would suddenly fall, then with great effort get up again and plunge at every one. In the evening she became more violent; she suddenly dropped to the ground as before, and seizing her front leg between her teeth, began to crush the bone and tear the flesh from it. She then got up, the blood streaming from her wounded leg. Again she fell and began chewing her leg, whereupon she was shot."

In *cattle* the symptoms are sometimes like those of the horse. The animals bellow often and loud in a hollow-sounding voice, show signs of mental derangement, stamp and butt so violently as to break off their horns. They seldom bite. Paralysis occurs and they die after from four to seven days.

A cow was reported to have been bitten on its nose, July 23d, 1893. On September 28th she carried her head up and her eyes had a wild stare. September 29th: She stopped eating and drinking and followed another cow around all day. September 30th: She could not eat, drink, or swallow her own saliva; what she did not blow out when bellowing dribbled from her mouth. Bellowing almost constantly; voice not unusual. October 1st: Bellowing somewhat like the voice of an ass; cannot eat or drink; looked wild out of the eyes; seat of bite red and congested. October 2d: Sore opened up and very red; voice better. In the evening drank about one quart of water; was brighter but would at times drop as if struck with an axe on the head (this is a peculiar sign); is now eating a little. October 3d: Drank a bucketful of water; ate corn, apples, hay, cabbage; redness all gone and sore closing. Throat swelled from ear to ear; she could not get her head

down; voice of pharyngitis. October 4th: Respiration difficult, incessant bellowing; could not eat or drink. Throughout attack would fall if an attempt was made to milk her; no evidence of viciousness, no paralysis, no spasm. Three other cows had like symptoms. Died October 5th. Post-mortem examination: Body warm internally. Very little rigor mortis. Ulceration (?) of pharynx, larynx, and trachea. Ulcers have an irregular contour and a yellowish-white membranous deposit. Dirt and a nail, which had punctured, were in the third stomach.

It is very doubtful if this cow would have been regarded as rabid from the symptoms alone. The only sure diagnosis is that based upon experimental inoculation. The case just related is in many respects atypical. The following is in most respects typical of furious rabies. Both of these cases were attended by William R. Tatum, D.V.S., who says: "I was called to see the cow because she was reported to be in labor and making no progress, and furious with the pains. She was bellowing almost constantly in a peculiar manner. I found the cow charging on a straw stack, as with intent to heave it down. She had gone through two fences to get at it. It was about seven hours since they had noticed anything wrong; she had been growing worse all the time. She was a young cow and I saw no sign of parturition; asked why they so thought, they said wait and you will see the calf's head. I had not long to wait before a pain came on, shaking her slightly from the head to the hind extremities (tremor ?), then followed spasmodic contractions of the abdominal muscles, especially the recti. At this the rectum opened and air rushed in; at the same instant there was a prolapse of the vagina with the os uteri in the centre, which they mistook for the calf's mouth and nose. The os was firmly closed; there had been no escape of liquor. This lasted a second, only to be repeated in quick succession, or after an interval of several minutes. The cow was bellowing constantly when not charging at something. The bellowing had a jerking rattle, I think due to saliva in the pharynx and larynx, which ran from the mouth and could not be swallowed, although frequent attempts were made, producing a sound more like the bray of an ass than that of a cow. On approaching her she made toward me, and I halloed at her, when she dropped to the ground as if struck in the head. I was at once struck at the similarity of this fall and the fall of the cow whose history was previously related, and she like the other at once got up again almost as quickly. This fall is more of a sudden dropping straight down and backwards, landing the body a little back from where it was, than anything else that I can describe. We removed the cow to a pen and gave her a bucket of water. She

made a number of attempts to drink and was apparently drinking, but none left the bucket. Soon she began to fall and get up again and try to drink; and every time she would try to drink she would fall. After doing this a few times she got up and charged on the bucket, running one horn through the bottom and became very much excited, fell down, and had a short tonic spasm followed by a clonic one in which the vagina was prolapsed more than at any previous time. I asked her owner to bring his dog down; the dog was no sooner seen than she dropped and immediately regained her feet and started for it, and came against the enclosure with such force as to break the rails. I tried her on some corn which she ate with great difficulty, until some chickens ran in to get their share of it, when she became again furious, charging at them and falling. The owner said that a dog had bitten a number of his cows and that a heifer was sick and would fall like this cow; but at no time was she violent, and drank milk up to the day of her death. The cow was shot. I did not make a post-mortem because my hands had fresh sores on them. I opened her mouth with two sticks, and found part of the tongue and back part of throat bluish as though the blood had stagnated there." Cattle die in from four to seven days.

In *sheep* and *goats* the symptoms are like those of cattle; they make unnatural leaps, butt eagerly, soon become thin, and die paralyzed in from five to eight days.

Swine at first show fright; they hide away and become greatly excited by noises; they are wild and very dangerous. The disposition to bite is very great, and they tear first one ear and then the other. Respiration is accelerated. The visible mucous membranes assume a leaden hue, as does also the superficial integument. A viscid foam is discharged from the mouth and the eyes glisten. Death occurs in from two to four days.

Cats are timid and their symptoms difficult to observe. They are very uneasy, run about excitedly, and tend strongly to bite. Death results in from two to four days.

The *domestic fowl* when attacked with rabies manifests great uneasiness, springs about wildly. A hoarse voice is noticeable; also a certain tendency to bite and finally paralysis (Bollinger). Only the last two words are correct according to my observation. The following is from Suzor: Rabies in our hens never showed any violent symptoms, but only a degree of sleepiness, loss of appetite, paralysis of the legs, and frequently a considerable degree of anæmia or bloodlessness as shown by blanching of the comb.

A word of caution relative to experimentation. On one occasion I trephined a hen and injected subdurally some of the egg of a rabid

hen. After a long incubation the hen became drowsy, gasped croakingly, and was pale in the comb. Most marked paralysis took place, and the case might have gone on record as inoculation of rabies from the egg had not the beak been opened and the membrane of diphtheria detected.

Wild animals lose their dread of man, whom they attack in remote settlements and outlying military posts. This applies to the wolf, fox, jackal, hyena, ferret, and skunk. Sometimes they make their way into villages, cities, and even houses. Many wild animals that die of quiet rabies and the paralytic form escape observation. The disposition to swallow unnatural substances is observed only in case of carnivorous animals. There is no aversion to water; they lap it unless prevented by affections of the organs of swallowing.

The diagnosis of rabies is not to be excluded, because on post-mortem examination another disease is discovered. I examined a dog that had bitten a policeman. The right side of this dog's heart was full of balls of the long slender worm called filaria imitis. These worms filled the cavity and projected into the vessels. The stream of blood was, as it were, filtered through them, but there was no fibrin, and no coagula were found. These worms were alive. The rabbits trephined from this dog developed rabies, and the man was treated. He is now well after several years.

Rabies in Man.

Rabies in man seems not to have been known until about 200 B.C. At this time in the writings of Celsus the word hydrophobia occurs. At a later date Plutarch, Pliny, and others describe the disease. Cœlius Aurelianus questions whether hydrophobia is a disease of the body or mind. Rabies was greatly feared by the ancients. They dreaded lest they should be bitten by persons suffering with the disease, imagining that if they came in contact with them the disease could be imparted. Even as late as 1840 those suspected of having rabies on the Austrian frontier were shot by their neighbors; and fifty years ago people were not unfrequently smothered when affected with rabies. "Rabies in man is an acute infectious disease, uniformly fatal, produced only by the implantation of a specific virus." In 90 per cent. this is the result of a bite of a rabid dog; of a cat, 4 per cent.; a wolf, 4 per cent.; a fox, 2 per cent. These bites are seated in 53 per cent. on the upper extremities, 28 per cent. on the head and face, 22 per cent. on the feet, and 3 per cent. on the body or scrotum. To cause the disease it is necessary only to abrade the epidermis.

It has been stated before that the disease can be conveyed during its

incubative stage in the dog. Every wound made by a stray dog that has escaped should be regarded as suspicious and treated accordingly. Accidental wounds producing rabies, as during post-mortem examination of rabid animals, have as yet in only one instance been satisfactorily proved. A student who had a small wound on his finger made an autopsy of a dog and died of rabies. This occurred in 1857 at the Veterinary Hospital in Copenhagen (Bollinger).

The *period of incubation* is uneventful; seldom it is less than fourteen days; rarely, if ever, over eighteen months. In the young it is shorter than in the old.

After the expiration of the incubative period, which, it is asserted, may be shortened by excesses of various kinds, by cold, by hardship, by passion, the patients complain of loss of appetite and headache. They are in a state of depression and gloomy agitation. If questioned as to any bite they may have received they affirm that it is of no importance, and has nothing whatever to do with their malaise. They become ill-tempered, apprehensive, excitable. There is a mental disquietude by which they are driven about, without any definite object, or they make a journey to relieve their nervousness by change of scene. They are often intensely anxious, contend against the idea that the bite is the cause of their uneasiness. In many cases they do not hesitate to deny that they have been bitten. They suffer with sleeplessness, and when sleeping have bad dreams. Many patients at this period are aware of the dangerous character of their disease, speaking frequently with a quick and sharp articulation of the coming serious ending. About this time a not uncommon and a very significant symptom is an aversion to fluids. M. Trousseau relates that he was at one time called in great haste to a patient who was suffering from what was termed an indigestion of water. The patient complained of intense thirst and was firmly bent on drinking, but could not carry water to his lips without being seized with a deep feeling of terror. He could not take solid food either. This difficulty of swallowing after slight malaise in a man aged thirty-seven years was a strange phenomenon. This sign marks the beginning of the second stage of rabies.

Stage of Melancholia.—The first stage is designated as the stage of melancholia, which may be very short. The patient is sad, silent, avoids company. There may be itching or pain at the seat of the bite, even though it is quite healed. This first stage seldom lasts more than four or five days. Sometimes there is a desire to walk or run, which is a sign of mental irritability rather than of melancholy.

Stage of Excitement.—In the second stage the breathing becomes

difficult, labored, sighing. The muscles receiving their nerves from the medulla oblongata become affected, producing spasmodic contraction of the pharynx and larynx. Hyperæsthesia of all the senses may occur—dread of water, of bright objects, of draughts of air, odoriferous substances, and noise or sound. There are hallucinations of sight, hearing, and smell. The feeling of suffocation and the hallucinations cause the patient great anxiety and excitability. These paroxysms sometimes appear like maniacal attacks with delirium. They come on usually at the height of the disease, and the patient becomes furious at those about him, striking and insulting them. These symptoms are not usual nor do they last long. Afterwards the patient expresses great regret at his behavior. At times in this excited state he makes snapping motions with his jaws. The convulsions vary from the slightest to the most severe; they assume both the clonic and tonic form. On the second or third day the very characteristic sign known as sputation is present. The matter ejected is just ordinary saliva, and this the patient may spit in little pools about the floor or eject to some distance, even into the faces of the bystanders.

A man bitten in September, exhibited symptoms of rabies in January. A little girl and another man bitten on the same occasion developed no disease. Previous to January he had been unquiet, sad. He made a journey from home in search of recreation, when suddenly a few hours after eating a breakfast with good appetite he complained of very intense thirst, was seized with general shivering, lost his appetite, could not swallow fluids, and was much agitated. This lasted for about thirty-six hours. General hyperæsthesia now took place; he could not wash his hands or face, any attempt to do so bringing on great agitation and violent shivering. This also occurred when he tried to comb his hair or beard. He dreaded touching his person with his own hand. There were rare intervals of quiet. To the skin hyperæsthesia there were superadded a very acute and frequently repeated excitation of the genital organs, frequent erection, and seminal emission. Three days after the invasion of the disease his aspect created alarm; he was agitated, garrulous, speaking in a curt, jerking manner. He could not drink, although he was very thirsty, and when he attempted to doze he was immediately seized with clonic convulsions and spasms. The hyperæsthesia and satyriasis persisted; the convulsive paroxysms became more frequent and he died on the fourth day, without having manifested any mental disorder or any hallucination of sight or hearing.

The above case illustrates many of the symptoms of rabies, the peculiar symptom satyriasis being very pronounced. Nymphomania has sometimes been noted in women. These symptoms are generally in the stage of excitement, but in the case related above the sexual ex-

citation existed in the prodromic first stage. There was not the least trace of the bite on the hands of this patient.

The most important of all the signs of rabies is the peculiar spasm of the muscles of deglutition and respiration, which make their appearance when water is presented. The water is dreaded because it suggests *immediately* the act of swallowing; food requires a precedent mastication. If air from a fan, from a window, or from an opening or closing door becomes dreaded because of producing convulsions, the affection is called aerophobia. The duration of the hydrophobic paroxysm is very variable, the spasms are short in duration and rarely extend over a space of time greater than from one-half to three-quarters of an hour. They come on suddenly. The quiet intervals are at times brief and hardly observable; at others they are prolonged to several hours. The intensity of the paroxysm is influenced by the sex, age, and individuality of the patient and by the mode of treatment. In females and children the attacks are milder. The patients can be quickly quieted by a quiet manner and voice. Their excitement is increased if those about them are agitated or if force be resorted to. Sometimes the paroxysms are completely absent. In their place are dyspnœa and deep sighing in the attempt to swallow; at other times the patient complains merely of great anxiety and obstructed respiration, and it is only shortly before death that a few convulsions take place. In exceptional cases the patient is able to swallow fluids during the whole course of the disease, although the act is painful; or, having been unable to swallow, he regains the ability to do so and this excites delusive hope of recovery. It often happens that he can drink with an effort, however, if he be not looked at, if those about him go away, if he closes his eyes, or if he sucks through a straw or tube. Warm drinks, milk, soup, and also wine, are often more easily taken than water. In by far the greatest number of cases there is inability to swallow anything. The attempt causes attacks of suffocation, respiratory spasm, and also spasm of the muscles of the face and neck and of the whole body, together with great mental disturbance. There is inability to take solid food, except with, at times, great difficulty. The spasm of individual muscles and of the muscular system in general is usually of a clonic character; rarely are there tetanic convulsions, and a decided tetanus or trismus has never been known. In the intervals between the attacks the intellectual faculties and consciousness remain as a rule unimpaired, although the tone of the voice may be much suppressed, and the patient is extremely anxious, disturbed, and talkative. There is insomnia except under narcotics. The intellectual faculties are in some cases disturbed. The patients see objects, animals, and men that are not present and hold imaginary conversations.

They imagine that others are responsible for their illness or they energetically defend themselves against imaginary insults and assaults. In a case in which there were marked priapism and emissions with voluptuous sensations, the patient in his delirium bitterly reproached his medical attendant for having recourse to witchcraft, in order thus "to take away from him the very principle of life." The disease of this man had set in with a fearful spasm as he was about to wash his face. He was a soldier and had been bitten forty days previously by a very small dog that had entered the barracks.

The patient's range of ideas is very limited, bringing forward the same ideas in a short space of time in the same manner. Maniacal attacks are in many instances attributable to rough treatment and attempts at restraint, or they are the result of the horrible anxiety and distress caused by the feeling of suffocation. The attempts to bite are merely actions of despair. The conjunctivæ are injected, the pupils dilated, and the retina is hypersensitive to light; the expression may be wild, agitated, and excited, or stupid and dull. The pulse is full, moderately strong, and accelerated, becoming weaker and quicker after the paroxysm. The skin is moist and perspiring. Respiration is normal during the intervals, but in the paroxysms it is gasping, irregular, rapid, and dyspnœic. The convulsive respiration is like that produced by a cold-water bath and is regularly attended with throat spasms; these come on together or the respiratory difficulty may come first. Thirst is decided and there is burning pain in the throat; the appetite remains frequently unaffected; the tongue is usually moist and clean. Sometimes there are convulsive eructations and vomiting of a coffee-ground substance; constipation is usual. The urine is small in amount; it never contains albumin, but sometimes sugar is present. The duration of the second stage is seldom as short as one day or as long as four.

The third stage is usually so short as to suggest a doubt of its presence. The fatal termination may take place very soon after the coming on of the severe convulsion. Death may be preceded by a state of general paralysis; this state lasts from fifteen minutes to a half-hour. The transition from the second stage is quite gradual, the convulsions becoming feeble and then ceasing. The patient is oppressed with forebodings of impending death. Consciousness remains until just before death. Death may take place suddenly in a convulsion from asphyxia, or quietly in coma. Some patients just before death are able to drink freely. The temperature rises as in tetanus and may increase for one hour after death up to 43° C. (109.4° F.). "Death is due to paralysis of the respiratory and circulatory centres. Rabies in man may be confounded with hysteria, tetanus, epilepsy,

delirium tremens, and acute mania, also with uræmia. In rabies the temperature is said to rise as death comes on; in uræmia it always falls. The type of the convulsions, the mental disorder, the abnormalities of general and special sensibility are very different in the two diseases" (Suzor).

Pseudorabies, Lyssophobia.

There is such a thing as pseudolyssa, and it may occur in those who are the subjects of some grave disease of which they die, and the deaths are ascribed to lyssophobia—in other words, they are said to be frightened to death. We may be sceptical as regards cases which are reported to have succumbed to lyssophobia pure and simple. In certain forms of neurasthenia the subjects imagine they have any disease that is brought to their notice; every lecturer on medicine is familiar with these cases in students. In a lacrymose way they tell us that they are sure they are taking rabies and they cannot swallow, yet the stomach tube is easy of introduction. But to do this in a really rabic patient is apt to result as in a case described by Trousseau. One of his clinical assistants, with the aid of several pupils, introduced an œsophagus tube through the nares into the stomach. About seven ounces of broth were gently poured into it. Half of this had reached the stomach when the fluid suddenly ceased to run. The tube was compressed by violent spasm of the pharynx and œsophagus. The spasm spread to the respiratory muscles; the face turned livid, the open eyes stared. The tube was quickly removed, and as the patient who had been sitting on a chair slipped down on the floor like an inert mass, it was thought that he had died. Water was sprinkled in his face, his tongue was drawn out of the mouth, which was kept open by firmly drawing down the lower jaw; the thoracic walls were alternately squeezed and left to expand. A whistling inspiration then followed, compression of the chest was kept up, and respiration was soon reëstablished, after which the patient ejected to some distance a quantity of saliva or bronchial froth. During the paroxysm there had been erection of the penis with ejaculation. The patient evinced no fear on finding himself lying on the ground. He knew that he had just run a great danger, but he believed that he had been saved. In the course of the evening he had several convulsive paroxysms and died suddenly. A post-mortem examination was made next morning. The body was very rigid, the face livid. The brain and parenchymatous organs were congested. The mucous membranes of the mouth and pharynx were very markedly injected. The salivary glands and saliva taken during life were sent to Alfort, but the dog inoculated took no disease.

A mayor of one of the French departments informed Trousseau that he had had rabies. A farm dog had tried to bite his arm, and had bitten a good many beasts which afterwards died of rabies. On Easter Sunday at breakfast, at which he had done his best to make up for a rigid lent abstinence, the mayor suddenly exclaimed that he had hydrophobia. He could not eat or drink any more and was already beginning to rave when his wife, who believed that he had eaten too much, persuaded him to tickle his throat with his fingers. Copious emesis took place and nothing more was said about rabies.

Trousseau related the case of this gentleman to a judge, who thereupon said that he also once imagined that he had hydrophobia. Riding on horseback one day, his favorite dog jumped up and kissed his hand; then he ran after sheep, biting all he could. He still heard and obeyed his master's call, but he had a strange aspect. Again he ran after and bit dogs, cows, oxen, swam a river, and died in a few hours. The judge heard that several of these animals died of rabies; he then remembered that the dog that same day had several times licked his right hand. On examining his hand he found several small scars upon it, and upon this was seized with terror. He no longer dared to touch water, to shave himself, and fully believed that he had hydrophobia. A physician tried in vain to calm his fears, and for several days he was excited and delirious. At last being told over and over again that persons with rabies died rapidly, that his dread of water dated ten days back, and after reading about the duration of hydrophobia, he allowed himself to be persuaded, and his dread of water vanished as soon as he became convinced that he should have died long ago if he had been rabid.

Paralytic Rabies in Man.

The paralytic form of rabies also occurs in the human subject; though much less frequent than the form just described, it is not extremely rare. The following is one of some thirty cases, reported by Gamaleïa.[10]

Nicholas Schegowitch, aged 12 years, was bitten August 26th, 1886, by a dog (not known to have rabies) in the right hand. No preventive treatment. The patient fell ill on October 4th with high fever, headache, and pain in the wounded arm, which was much swollen. The following day he had pains in the stomach with vomiting. The following night he was restless, talking and walking during sleep. The succeeding days the same condition was noted. The patient, however, was able to eat and drink.

Patient arrived at Odessa October 8th. He had total paralysis of the right arm, slight facial paralysis on the right side and signs

of the commencement of paralysis of the respiratory centre. Sighing respiration, heavy inspiration; when a draught was present, hiccough, uneasiness, and fright. Temperature, 37.7° C; evening temperature, 39° C. Pharyngeal spasm during eating. At times the patient had periods of excitement and began to cry and complain.

He was delirious that night. There was profuse ptyalism, fully six ounces of saliva being excreted. In the morning he complained of pain in the lower extremities and there was paralysis of the right leg. Temperature, 36.5° C. (97.7° F.). The boy was able to eat apples and raisins. In the evening of this day (October 9th) the temperature rose to 38.3° C. (101° F.), the paralysis had increased so that the patient was no longer able to stand, there was ptosis, and the patient was delirious at times. The next day the symptoms were about the same. There was no pharyngeal spasm, but complete paralysis. Towards evening dyspnœa became marked. On October 11th the morning temperature was 37.7° C. (99.9° F.). Divergent strabismus was observed and there was paralysis of all the muscles of the body, the patient remaining immovable until death, which occurred at 4:30 P.M.

The following case is in contrast to the foregoing:

Dr. Sappington did me the honor to call me in consultation with regard to Wm. Glavesky, age 14 years. This was on February 6th, 1895, about 3 P.M. The lad was on a lounge in a semi-erect posture, supported by his father back of him. His brown irides were widely dilated, but responded to light slowly. The eyes were brilliant, the anterior chamber seemed deep as though overful of fluid. Pulse rapid, tongue clean. He could not swallow water. Air blown on him, or rubbing his extremities, was abhorrent. He complained of his father's breath on his head; objected to the proximity of those about him, saying that their breath was fetid; heard noises in his ears as of bells; carried on an imaginary conversation with his sisters, who were not present. During or just before a spasm, he thought he saw black things and attempted to repel them. He was constantly spitting ordinary saliva, forming little pools about the floor, and for this untidiness he apologized to his mother. He tore his body with his finger nails in scratching, because of intense itching, which he also had in his nose. At intervals of five or ten minutes he had a clonic convulsion, struggling in the arms of his father; this passed off with rigidity of the extremities, the boy stretching himself tetanically for an instant; he did not seem to have lost consciousness. Afterwards came a period of remission. He got off the lounge, adjusted his clothing, shook hands with his visitors, and remarked to me "I thank you for coming to help my father." He walked about the room, went to a window, and waved his hand to a neighbor. To his pastor asking to visit him, he replied, "I will if I live." He put his hand to the back of his head and said he had pain there, also in his epigastrium and hypochondria. The first symptoms appeared on February 1st, when he complained of stiffness at the back of his neck. Following this he had headache, stiff neck, some choking, gasping, and short

breath, slight cough, and pain in the epigastrium; he could not eat or drink, but attended school.

On February 6th, shortly before I saw him he fell down. This tendency to fall is remarkable, and occurs in animals as a result of incoördinate muscular action present in rabies. That night he died after convulsion. Here was a strange contradiction of symptoms! Looked at in the light of fear, he was very ill; viewed in the light of hope, his condition did not seem desperate. He had been bitten by a stray dog on the right hand, dorsum and thenar eminence, about November 24th, 1894.

The following case is in contrast to that of Gamaleïa. It is one of the Baltimore cases hereinbefore mentioned. I had the honor to see this case by invitation of Dr. C. H. Mitchell and in company with Dr. R. B. Norment.

Conrad Eppers, aged 15 years, was bitten on the back of the neck (wounds severe and multiple) on December 1st, 1896. Underwent Pasteur treatment in New York. Date of first treatment, about fifty hours after the bites. Discharged from treatment December 17th. There had been no efficient cauterization of the wounds. He died of paralytic rabies, December 26th, nine days after termination of the treatment. Dr. Mitchell saw him on December 23d. He was quite nervous, but being naturally so this was not regarded. On December 23d he was found to have marked facial paralysis, dilated pupils, and unsteady gait. I saw him on December 25th; he had complete ptosis of the left eyelid, he could not shut his mouth, could not inflate his cheeks, could not whistle, could not expectorate, but continually thrust a handkerchief into his mouth in order to mop up and remove the excessive salivary secretion. Attempting to walk, his feet would swing about in an incoördinate way. He had had pain in the wounds on his neck. When asked to drink water, he evinced no dread; he simply refused and said that he would not try. His countenance expressed deep gloom; whether due to paralysis of the muscles of expression or a reflex of his mental condition was not determined. Dr. Norment stepped behind him, out of his observation, and fanned him gently; instantly he sprang from his chair in terror, struggling for breath. As the spasm passed off he took a long, sighing inspiration. His physician saw him two hours before his death, and reports that he had at no time convulsions, but was simply in a paralytic condition. He also vomited almost incessantly during the afternoon. Dr. Mitchell remarked that in both cases (referring also to a lad named Henry, who died from a bite of this same dog) the extremely dilated pupils, the fear of something, the anxious countenance, and the black vomit were noticeable signs; this vomit was copious in another lad named Perry just before his death, at which time I saw him. It is like the vomiting which takes place in septicæmia. I have observed this dark fluid at times in the stomach of rabid dogs; it is probably bile.

Trousseau, quoting Van Swieten, remarks that in the human sub-

ject death always occurs within four days after the first rigor and difficulty of deglutition have set in. Most patients die of asphyxia, but in one man death was not preceded by convulsions or even by struggles, and seemed to result from general paralysis, "as though universal paralysis ushered in death."

The boy Henry, aged 8 years, was bitten on his left cheek, December 1st, 1896. No efficient cauterization. Date of first treatment, seventy-seven hours after the bite. Date of death, December 21st, three days after termination of the Pasteur treatment in New York. He had been discharged from treatment on December 18th, and was then well, very tired, and thought he had taken cold. Dr. Mitchell saw him on Sunday, December 20th. He was rested then, but his mind was in a stupid condition and he did not want to be disturbed. On Saturday he had played about as usual. He came in Sunday afternoon, and his mother noticed that he was very irritable. He had gotten up early that morning, still complaining of being tired and of earache. Within an hour his symptoms had become extremely aggravated. He would seem to be perfectly conscious, and then in a moment make an irrational remark. He was offered a drink, and it was impossible for him to take it. "He did get down one swallow with a terrible gulp." On the next day he looked like a child that had been ill for a great while.

When I saw this child, who was a bright, brave, little fellow, he said to me: "I suppose you have come to kill me. I suppose all the boys must be killed." This was the result probably of conversations held among the boys relative to what would be done with them should they go mad. He was delirious one instant and rational the next. His condition of tremor and excitability verged on convulsions. He was asked to try to drink a mixture containing bromide of potassium and chloral. He did try; as his trembling hand carried it to his lips, with eyes staring and muscles of his face working spasmodically, he did get some drops into his mouth, remarking with great satisfaction: "Yes! yes! I did swallow some of it." This was about 11 P.M. He died the next day at 5 P.M., after a severe convulsion, of which he had had previously quite a number. The rapidity with which death supervenes after the oncoming of nervous symptoms is remarkable.

The two foregoing cases and the following case were experimentally demonstrated to have had rabies by inoculation of emulsion of the medulla oblongata subdurally into rabbits. The case about to be related was attended by Dr. William E. Magruder, and reported by William E. Magruder, Jr., Olney, Md.

Resin Perry, aged 67 years, was attacked, February 3d, 1894, in the public road by a small dog, which appeared to be rabid. While actively fighting and running backwards, Perry fell on a pile of stones and continued resistance on his back with the dog over him. He found a slight wound over his left eye, and at the time thought he had received it in his fall on the stones, but soon his eye inflamed

and remained very sore for several days, when it gave no further trouble.

After talking with some friends he became somewhat scared, and feared that he had been inoculated with rabies. On April 11th, the eye again bec ame much inflamed, pains radiating from it over the side of the head · ad neck, followed by pains in the abdomen and limbs. He complained of being unable to sleep and of inability to drink water the night before, although suffering from excessive thirst. On the 13th spasmodic contraction of the diaphragm occurred, and the idea of swallowing became abhorrent. On the 14th inability to swallow was complained of, and even the suggestion of drinking gave what he expressed "a pain in the stomach and takes away my breath," and said if he could only take some medicine which would enable him to drink he would get well. When induced to attempt to drink, he would scream and run across the room, imploring that the water be taken away from him and out of the room, returning soon to the couch, exhausted and out of breath. The same phenomenon was produced when the door blew open and when the physician washed his hands in the room. The patient frequently expressed surprise at his condition and wondered at the cause, laughing at jokes and joking between the paroxysms. Pupils contracted. Hypodermic injections of morphine and atropine, and tablets of the same were left with directions for their use at short intervals. On the morning of April 15th the patient seemed more quiet than before, but had slept little during the night, having numerous paroxysms followed by rational intervals. Respiration was labored, pulse 110. The temperature was taken only once, when it was normal, and this was the day before death. There was no excess of heat at any time perceptible to the touch.

I administered thirty grains of chloral by the rectum and fifteen drops of fluid extract of gelsemium, with morphine, gr. $\frac{1}{4}$, and atropine, gr. $\frac{1}{150}$ subcutaneously. Ordered twenty grains of chloral per rectum every two hours until the man became quiet, but after the fourth dose the nurse could not administer it, as characteristic spasms were produced. Chloroform was used, but discarded for the same reason, as it produced characteristic spasms after a few inhalations. One grain of morphine and $\frac{1}{36}$ grain of atropine with fifteen drops of fluid extract of gelsemium were administered hypodermically, and the dose was repeated every two hours until the patient became thoroughly narcotized, since all the attendants were afraid of him and he had become unmanageable. Until near the last of the attack there was almost constant spitting of viscid sputa. He was seen at four o'clock in a profound stupor, pupils slightly dilated, pulse 120, respiration deep and slow, face occasionally twitching, and extremities cold, with muscles completely relaxed. He took no food, but drank a little water on the 15th and 16th, amid spasms and screams. He remained narcotized until 4 A.M. on the 17th, after several doses of the anodyne had been neglected, when he left his bed and walked across the room. Injections of anodyne were resumed and repeated in twenty minutes by the nurse, who had become frightened, and were continued every two hours until ten o'clock, when they were discontinued. Stupor returned after four

o'clock, and he gave no further trouble. At eleven o'clock the pulse was 124 and compressible; respiration, 16 and shallow. At 4 P.M. the pulse was stronger and stupor less profound, but the mouth was dry. Anodynes were again administered and repeated when indicated until his death at 12 P.M. on the 17th. There was no general spasm.

A section of his medulla oblongata was sent to Dr. Keirle, of Baltimore, who trephined and injected subdurally two rabbits on April 19th, with emulsion of this medulla oblongata rubbed up in bouillon; both rabbits developed rabies on May 3d, and both died May 6th.

Gamaleïa's cases of paralytic rabies were generally the result of deep and multiple bites. The onset was marked by strong fever, general malaise and aching, headache, and vomiting, as in all acute infectious diseases. Such an onset is very frequent also in ordinary rabies. At a certain period of the disease there is a high degree of fever; as the disease goes on there is an occasional morning remission and evening rise, but the temperature not a great while before death may rise above normal, and thus persist up to the time of death, and rise somewhat afterwards; or at the time of death the temperature may be almost normal, 37.7° C. (99.9° F.). The characteristic temperature fall which occurs in the rabbit experimentally inoculated subdurally, and which with very rare exceptions continues up to death, is not the thermal phenomenon of paralytic rabies in the human being and not that of rabies in general in the human species, in which, though a fall below normal may occur during the course of the disease, it is more of the nature of remission, for the temperature rises again and registers even more than 40° C. (104° F.); a progressive elevation to this degree indicates impending death (M. Schaffer). Subsequent to this advent comes a train of localized pains, generally in the limbs bitten, and girdle pains at different heights of the vertebral column. These localized premonitory pains are rare in the lower limbs. Next supervene a degree of numbness of the senses, fibrillar contractions, ataxy, paresis, and then paralysis more or less complete of the muscles first implicated. General sensibility remains intact, or if it disappears it does so very much later. Then the paralysis spreads, preceded or accompanied by sharp pain in the muscles invaded; the remaining limbs, the trunk, the rectum, the bladder, the face, the tongue, the eyes, are all paralyzed. So also, sooner or later and more or less completely, the respiratory centre, the implication of which brings about a marked change in the inspiratory phase of the patient's breathing; and as a corollary, some difficulty in swallowing liquids (the so-called great symptom of hydrophobia, or horror of water, being a result much more of the imagination of the patient and of the medical man than of the rabic

virus). But the incoördination and spasm of the muscles of deglutition and respiration in rabies are not imaginary; they cause a fearfully real choking, and anything that suggestively calls into action these muscles is avoided and dreaded by the patient. When well marked, this respiratory lesion is the cause of dyspnœic convulsions in the muscles which are not yet paralyzed. Then there is frequently a return of the breathing to the normal, but with it is a spread of the paralysis to the heart with death by syncope. This form of rabies has a duration of seven and a half days on an average.

Pathology.

The gross pathology of rabies presents nothing of specific character, nothing that is not usually present in death from infectious diseases. In man and the dog certain gross lesions correspond, such as pial hyperæmia, cerebral and pulmonary œdema, and vascular injection of the upper part of the œsophagus and of the larynx and trachea; the latter is, however, often not well marked, and is not the cause of the altered voice, which is of nervous origin. The follicles of the tongue and pharynx are not infrequently enlarged; but according to Virchow, this is quite frequent in rabies in man. The pharyngeal follicles and lymphatic glands in the neighborhood of the jaw are swollen. The pharynx and epiglottis are usually of a deep red color, but are often also quite normal. The lungs are studded with points of atelectasis and hemorrhagic infarction, together with sanguineous effusions beneath the pleura. In the dog there are areas of lobular pneumonia due to foreign matter inhaled. Klebs found intense redness of the ulnar, axillary, jugular, and inguinal glands, the tonsils, and lingual glands. Peyer's glands, as a result of swelling and redness of the outer follicles, presented a peculiar wall-like appearance. Upon microscopic examination there was found in all the swollen portion of the lymphatic, and particularly in the submaxillary gland, a deposit of finely granular, highly refractive corpuscles, of faint brownish color, closely packed together in clusters, at some points in the form of long rows, in others branching out so as to form large star-shaped figures, following in general the course of the blood-vessels. These corpuscles, according to Klebs, may prove to be the vehicles for the transfer of the specific infecting material. This is an unsustained inference; for these bodies are probably the result of granular degeneration and subsequent change. The hyperplasia, granular degeneration, and ecchymoses are present in lymph structures in rabies, but they are also present in other infectious diseases, as has been before noted in the case of septicæmia in the dog. In discussing pathology

it is necessary sharply to differentiate matters of fact and matters of inference. The former, making some allowance for imagination and bias, are correct—so far as they go; but the latter can never be accepted at any time, except upon a basis of thorough experimental demonstration. These remarks have an application in the kidney in rabies, especially in that of the dog, in which the kidneys are livid and of a dark grayish-blue color. The inner zone of the cortical substance is usually marked by turbid yellow stripes, the result of fatty degeneration—a normal condition in the dog's kidney. The epithelium in the convoluted tubules is opaque and undergoing molecular degeneration. There is also albumin in the urine. From these appearances Reednew inferred that the pathological phenomena in rabies were the results of uræmia. The dark-blue cyanotic renal color is common in poisoning by alcohol and opium. In the human being the kidneys are hyperæmic, and the cortex is swollen, slightly opaque, and cyanotic. The bladder is usually empty.

Boulanger sums up the appearances as follows: Blood dark; œdema of brain; more or less pronounced catarrhal alterations of the mucous membranes, especially of the respiratory and digestive canals, conjoined often with hyperæmia and ecchymoses, hyperæmia and cyanotic discoloration of the parenchymatous organs; in dogs absence of food and presence of indigestible foreign substances in the stomach and intestines, together with emaciation. In herbivorous animals there is absence of all characteristic changes. In cattle the morbid appearances are often similar to those of cattle plague.

Suzor gives the following post-mortem appearances in rabies in the *dog:* Dark-blue and almost black color of the tongue and of the whole mucous membrane of the mouth. In the stomach some discoloration of the lining membrane; black liquid like coffee dregs and heterogeneous materials, not usually swallowed by healthy dogs, constitute the contents of the stomach. Some claim that these foreign substances are present in every case of rabies; another authority says in fifty per cent. of the cases. Congestion of the lungs and of the central nervous system and extreme retraction of the bladder are frequent, but by no means constantly present or characteristic. The hard palate of the dog's mouth is very often pigmented and this must therefore not be regarded as significant.

The foregoing description has a practical outcome in enabling one to answer the question, Is this dog mad? The dog in question has bitten other dogs and human beings; shall the former be destroyed, and what shall the latter do to be saved? You cannot wait fifteen or twenty days until the result of trephining or other method of animal inoculation matures. If there be foreign matter in the stomach; if the

lymphatic glands show ecchymoses; if the medulla oblongata, hardened in alcohol and stained with aniline red or other stain, exhibit the knots of hyaline degeneration about the vessels and in the cells regarded by Babes as characteristic—if all these appearances are present, there can be no reasonable doubt; if any one of them be present, or if the suspected dog or other animal has escaped, treatment should be advised. Should the experiment demonstrate that the dog was not mad, it is a mistake barren of consequences; on the other hand, if the dog be proven to have been mad and those bitten be advised against treatment, it is a mistake that may be followed by a train of calamity.

Post-mortem examination in *man* reveals the following lesions: Cerebral œdema, pial hyperæmia, redness of the membranes of the medulla oblongata and cord, sometimes decided softening of brain, medulla, and cord. The lungs are red, congested, here and there the seat of small hemorrhages, filled with frothy mucus formed at the time of death. There is interstitial and subpleural emphysema. These pulmonary lesions, like the liquid black state of the blood, seem to be the result of the terminal asphyxia (Suzor). Hemorrhages into the muscular tissue of the heart, parenchymatous nephritis, congestion and swelling of the lymphatic glands, with the terminal leucocythæmia, softness of the spleen and liver, with fatty degeneration of the latter—all these are the well-known lesions of infectious intoxication.

The following are the lesions found post-mortem in the case of the lad Robert Henry, previously reported on page 546:

Head—free bleeding on incision of scalp, also from the vessels on removing calvarium. Veins of pia and sinuses much engorged, cerebral œdema, hyperæmia and extravasation of capillaries of medulla oblongata and cervical cord. Pial vessels, veins, and capillaries very hyperæmic; here and there extravasations. Cortex on section darker than normal; vascular puncta marked.

Body: Subcutaneous fat absent. Pericardium contains 10 c.c. of a pale straw-colored fluid. Heart firmly contracted (rigor mortis?) and almost empty. Two drachms of blood in right auricle. Small amount of dark, partly clotted blood in left ventricle. Very little in right ventricle; dark-red clot in pulmonary artery. Lungs—marked hypostatic congestion; on section ooze bloody fluid freely, intense venous hyperæmia. Stomach—dark-colored fluid. Liver—limited yellow area (fatty degeneration), common appearance in septicæmia. Gall-bladder full. Kidneys hyperæmic. Pancreas apparently normal. Spleen dark-red, moderately firm. Œsophagus normal. Larynx and trachea normal, except that the latter is too pale, indicating perhaps intense hyperæmia during life. Bladder

empty. (The boy died at 5 P.M.; at this time, 7:30 P.M., it is noticed that rigor mortis is beginning.)

Conrad Eppers, aged fifteen years. The clinical history is related on page 545. Post-mortem examination twelve hours after death.

Free bleeding from the meningeal vessels; extravasations along the longitudinal sinus; also free bleeding from the pial vessels, which are very hyperæmic. Cerebellar cortex, on section, dark; cerebellum softened. Veins in vertebral canal very hyperæmic. Lungs œdematous, pit on pressure, ooze freely bloody fluid. Heart—one ounce of fluid in pericardial sac; coronary arteries full of blood. Dark fluid blood in right auricle; very little in right ventricle; left ventricle empty. Spleen—6 × 2½ × 1½ inches. Liver apparently normal. Kidneys very hyperæmic. Pancreas hyperæmic. Larynx contains frothy fluid; œdema over arytenoid cartilages.

The foregoing post-mortem examinations exhibit nothing specifically indicative.

Microscopy of the Nervous System.—For the following microscopical examination of the nervous system and other tissues of the dog and of the boy Henry, the writer is indebted to Dr. Standish McCleary, associate professor of physiology at the College of Physicians and Surgeons, Baltimore. In the gray matter of the cervical cord of the dog there are hyperæmia and extravasation; also escape of polynuclear leucocytes into the perivascular lymphatics. Granular degeneration of ganglion cells. In the nerve fibres the medullary sheath of Schwann is swollen and hyaline through the entire section. In the kidney blood is extravasated into and between the tubes; also from the glomeruli. The cells of the uriniferous tubes are very much enlarged and finely granular (cloudy swelling). The intertubular vessels are hyaline, and small round cells are proliferated in the connective tissue here and there. The lymph glands exhibit abundant blood extravasation; those in the axilla have the leucocytes pigmented occasionally. The ganglion cells of the medulla oblongata are swollen, their nuclei are granular, and the adjacent protoplasm is hyaline; hyperæmia and minute extravasations in the gray matter (dorsal accessory nucleus, olivary body). Some condition of hyperæmia and extravasation in the white matter (formatio reticularis). The vessels are hyaline, and there is extravasation of polynuclear leucocytes.

Suzor says that on post-mortem examination the lesions of main interest are found to lie in the central nervous system. The nerve cells are cloudy and granular; there is general congestion of the nerve centres, the blood-vessels being dilated and ruptured here and there, giving rise to small hemorrhages: miliary abscesses throughout the substance of the medulla oblongata, more sparsely in that of the brain

and cord; foci of finely granular matter infiltrating the normal nervous element, the perivascular lymph spaces, and the walls of the blood-vessels, which are compressed and assume a moniliform or beaded aspect; hyaline thrombi or blood clots form in the interior at the level of these compressed points, the whole giving the appearance of a nodule or small tubercle, in the interior of which Klebs thought he had discovered the specific micrococcus. There is frequently softening around the central spinal canal. Ross, of Manchester, finds that the lesions here are most marked, but the anterior and posterior horns and the gray matter throughout are largely implicated also, mainly so perhaps. He thinks there is similarity between the lesions of tetanus and rabies. In the former they are chiefly spinal; in the latter cerebral in their main localizations. This observation is perhaps not sustained. The ganglia of the sympathetic system and of the nerve roots show the same lesions as the brain and cord. The nerves, and in particular those of the bitten parts, those rising from the medulla—the vagi, the glossopharyngeal, the hypoglossal, the spinal accessory, and the phrenic—have been found red, hyperæmic, swollen, and the seat of minute foci of hemorrhage; the myelin is diffluent, fragmented, and in many nerve fibres the axis cylinder has altogether disappeared.

William H. Welch, of the Johns Hopkins University, says that serial microscopical sections of the medulla oblongata and pons from the second cervical nerve upwards exhibit small hemorrhages and accumulations of small round cells in large numbers, both in the perivascular lymph spaces and in scattered foci in the neuroglia between the nerve elements; hyaline thrombi and leucocytes in the small blood-vessels. These lesions are microscopical, and their extent and distribution can be determined only by the examination of a large number of sections from different parts. The lesions are especially well marked in and near the nuclei of origin of the spinal accessory, pneumogastric, and glossopharyngeal nerves, and in the motor nucleus of the trigeminus. Cases have been reported in which even more extensive lesions than these have been found, their intensity depending apparently in large measure upon the duration of the disease. While it cannot be claimed that these lesions are peculiar to hydrophobia, or by themselves suffice for its diagnosis, it is incorrect to suppose that hydrophobia is a disease without demonstrable anatomical lesions which bear a manifest relation to the symptoms of the affection.

Victor Babes,[1] treating of the histological lesions of rabies, notes the hyaline degeneration of the vessels and the presence of miliary nodules around the vessels and cells—"la présence des lésions décrites

et surtout des nodules pericellulaires parle en faveur de la rage de l'animal suspect." He also refers to inflammatory lesions, especially of the vascular tunics. Some of these lesions are visible to the naked eye, but usually they are not.

Dr. Henry J. Berkley, of the Medical School of the Johns Hopkins University, replied to my request for information regarding the lesions of rabies in the rabbit's brain as follows: "The lesions in the four hydrophobia rabbits I have studied are entirely similar to those resulting from other irritant poisons, but resemble more the alterations in chronic serum poisoning than anything else I have studied—namely, a peculiar swelling of the dendrites of the nerve cells, with loss of the gemmulæ, and eventually atrophic changes in the corpus of the cell." Berkley[12] quotes Golgi as follows: "In both cell body and dendrites there are evidences of decided alterations, in the form of circumscript or diffuse swelling, atrophic changes with loss of substance, a process of progressive atrophy which proceeds apparently from the cellular body to the finest extension of the protoplasmic branches. The processes are involved to their extreme periphery. The cells lose their homogeneousness, have a granular appearance, and show diffuse swellings which give them a varicose appearance. There is also an involvement of the axis cylinder in the form of a beaded swelling of the fibre. A peculiarity of the process is that the abnormal alterations of the elements are not diffused throughout every portion of the central nervous system, but they are focally distributed; thus one sees zones with altered cells and others without alteration of the nerve elements."

"Golgi," Berkley remarks, "is evidently inclined to think that the alterations above described are pathognomonic of rabies and that they are due to an inflammatory process, and gives this the name encephalomyelitis parenchymatosa." There is, however, no inflammatory process set forth in the foregoing quotation from Golgi.

As regards the vascular system, Berkley says: "I have failed to discover in the cortex of the rabbits any evidence of coarse lesion of the vessels in the form of extensive hyperæmias, plastic exudates, and extensive emigration of corpuscular elements into the perivascular sheaths, nor could a single extravasation of the red corpuscles be found as described by Popoff[13] and others in the human subject. None of the cortical vessels of the rabbits' brains showed more than a moderate filling of the capillaries, and but a trifling emigration of the polynuclear elements, and no extravasation of plastic exudate of any description. The perivascular spaces are only moderately wide, contain a comparatively small amount of finely granular débris, no hæmatoidin crystals, or indeed anything beyond a few lymphoid cor-

puscles. The latter elements are but sparingly present in the blood within the walls of the canals. The sheaths of the vessels are not greatly altered, the endothelial nuclei are not swollen, some of the nuclei of the muscularis show a tendency to absorb less of the aniline stain than usual and show vacuoles, but the muscular fibres are not swollen or hyaline, and, altogether, the evidence of a degenerative process taking place in the walls of the nutrient vessels is inconsiderable.

"We have, therefore, in the present cases only the indications of a mild infection, of sufficient intensity, it is true, to cause death after the lapse of a considerable number of days, but insufficient to produce any considerable morbid change of the vascular walls, together with a degree of leucocytosis such as is often found when the soluble poison of bacterial source acts with a considerable degree of energy upon the blood-forming organs.

"These conditions are therefore most favorable to enable one to ascertain the effect of the subtle poison from the rabies bacterium upon the nerve elements. Golgi's cases, in which he found karyomytosis of the nuclei of the vascular muscles, must have been of greater severity, and the damage to the nutrient supply has borne its part in the production of the nerve-cell changes, which we are now able to exclude to a certain degree.

"I can see no signs in any of the preparations of anything approaching an inflammatory process taking place in the cerebral tissues, only the indications of a purely degenerative reaction from the effect of a toxic substance produced by the bacterium of hydrophobia, essentially causing the same pathological changes as those induced by other soluble poisons when present in the circulation in sufficient quantity to disturb nutrition."

It must be borne in mind that Dr. Berkley is writing of the cerebral cells and cortex in rabies in the rabbit; if this rabbit was obtained from me the virus was probably fixed. It is necessary also to remember that the bacterium referred to is a supposititious one. That the rabic virus, be it what it may, is phlogistic is by no means certain. The appearances, conspicuous as they are, macroscopically or microscopically, are susceptible of explanation independent of inflammation. Toxineurosis, if the word may be applied to the organic changes produced by a poison in the nervous system, can independently and directly produce coagulative necroses. Infectious intoxication is not necessarily inflammatory or in this way toxæmic. So far as rabic intoxication is in question, the blood stream is only very transiently a carrier of it; only exceptionally and by inoculation of large quantities can rabies be produced by the blood. The virus of rabies can kill the protoplasm of cells and the

vessel wall. Whether the latter is killed from within or from the tissue and lymph stream without, is a question, but the results of experiment do not favor the former route. The hypothetical bacterium and its toxin are repelled by the blood. How does the blood deal with rabic virus when injected into the blood-vessel? This point may be approached digressively by a passage from Suzor: "M. Bouley remarked to Pasteur, 'Perhaps there is no such thing as a microbe of rabies.' 'All I can say,' replied Pasteur, 'is this, that if you were to bring me two brains, the one rabid and the other healthy, I could say from a microscopic examination of the two medullas, this one is rabid, that is not. Both show an immense number of molecular granules, but those in the rabid medulla are finer, more numerous, suggesting the idea of a microorganism of extreme tenacity, in shape neither a bacillus nor a diplococcus; they are like simple dots.' One method alone hitherto has allowed us to isolate these granules from all the other elements of the nervous matter. It consists in injecting the pure virus taken from the medulla of an animal which had died from hydrophobia into the veins of a rabid animal just at the time when asphyxia is coming on. In a very few hours the blood of the animal is found to contain exclusively the infinitely small granules we are speaking of, the normal elements of the nervous matter having either been stopped in the capillaries or having, more probably, been digested in the blood. It has also become easy under these new conditions to stain them with the aniline dyes."

With regard to the blood of rabid animals we have in one instance been able to give hydrophobia to a dog by means of the blood of a rabbit which had died of that disease. The granules in the blood described by Pasteur are not organisms, they may be the means by which the blood deals with organisms, the granules of certain leucocytes which destroy them and prepare them for removal by certain other leucocytes, or they may be the granular remains of leucocytes destroyed by the organisms or their toxic products. These may be the granules described by H. F. Müller.

Blood of Rabbit in Rabies.

The following is the report of an examination of the blood of a rabid rabbit kindly prepared for this article by Dr. Standish McCleary: "To ascertain what changes if any were produced by the laboratory (fixed) virus upon rabbits' blood, counts were made from healthy animals (rabbits) and from rabbits in the last stages of rabies. Differential counts were made from specimens stained by Ehrlich's triple stain and also by hæmatoxylin and eosin. The results could hardly be otherwise designated than negative. The number of red

cells per cubic millimetre in the healthy rabbit was found to be about 6,000,000, while the total number of leucocytes amounted to 7,500. The blood of rabbits in the last stages of rabies showed the erythrocytes reduced to 5,460,000, and the leucocytes to 7,200 per cubic millimetre. The percentage of hæmoglobin was proportionately diminished. This oligocythæmia was to be expected on account of the anorexia and general malnutrition concomitant with the disease. The absence of even the slightest leucocytosis is to be noted as indicating that there is not a meningitis or any suppurative processes in the nerve centres."

Contrast this condition of the blood with that which occurs in the toxæmia of rabbit septicæmia. The following is an account of the condition of the blood in the experiment in which the bacillus of rabbit septicæmia was derived from the medulla oblongata of a supposed rabid dog (see page 505). Special attention must be directed to the dyspnœa which is hæmic, not pulmonary. The lungs are pallid and bloodless, or, more correctly stated, the blood is not red blood, the red blood corpuscles are not red; even when closely agminated their color is only a faint yellow and the single corpuscle has no color at all. Morphologically the red corpuscles are distorted, fail to maintain their sphericity, and may, like a globule of mercury, drag a tail; in addition to this poikilocytosis there is a pseudo-nucleation caused by a circumscribed absence of protoplasm (hæmoglobin). This excessive liability to vacuolation of the corpuscles is general and takes place in different parts of the area of the cell. Sometimes the cell is emptied of its contents, the periphery alone as a mere ring remaining; sometimes, as just noted, a zone between the circumference and the centre is vacuolated, leaving the centre as a seeming nucleus; the term excessive liability has been used advisedly, because all vacuolation occurs as a post-mortem change, and as a result of reagents, specially acid stains (dyes); but this disintegration described, this granular necrosis, this proneness of protoplasm to drop out is an *intra-vitam* result of this organism, a pernicious anæmia.

Diagnosis.

The complete picture of furious rabies in the dog is not difficult of recognition, but unusual forms and paralytic rabies may escape the detection of the most careful and experienced veterinarian, who for its solution is compelled to resort to experimental demonstration.

In general, in man, continuous observation and a good clinical history obviate error. It is difficult to confound rabies, as it occurs usually in the human subject, with any other disease. A most

distinguished clinician has remarked: "Other diseases may be confounded with true croup, but when you see your first case of true croup, you do not confound it with any other disease." This remark is entirely applicable to rabies, as it generally presents itself. Certain forms of rabies, if observed disconnectedly, may be mistaken. Maniacal rabies, observed only in the maniacal period, may resemble ordinary mania if the previous history be disregarded. Hysteria lacks the reflex excitability of rabies. The symptom of black vomit is a late sign indeed, but it may suffice to distinguish rabies paralytica from Landry's paralysis. The usual form of acute tetanus cannot be confounded with rabies, the former supervenes within ten days of the reception of the wound; the sardonic grin is absent in rabies. Subacute tetanus with long incubation often terminates in recovery, and its persistent muscular rigidity is unlike rabies. Cerebral tetanus, caused by wounds in the vicinity of the cerebral nerves, in which spasm of the muscles of the jaw and throat takes place, has a shorter period of incubation; persistent spasm of the jaw muscle (lockjaw) is not a symptom of rabies. The temperature is sometimes relied upon to distinguish tetanus from rabies. A decided rise of temperature in the former is supposed not to take place in the latter, but rabies in man does have a decided rise of temperature which may portend death, as has been adverted to, and the temperature may rise in the rectum after death to 42° C. (107.6° F.). The temperature in human rabies "rises as death approaches, in uræmia it falls below normal."

Treatment.

That death must always result in order to prove the diagnosis of rabies in man is perhaps an erroneous assertion, but no fully demonstrated case of recovery is on record; of course the demonstration of the recovery is contingent upon the demonstration of the disease, which in case of recovery is very difficult. Allbutt quotes a case from Lebell and Venesco in a child six years old in whom the disease in a severe form supervened during treatment, which was interrupted and resumed on the abatement of the disease. In the treatment, in addition to the Pasteur series, fixed virus heated to 80° C. (176° F.) in emulsion was used in quantity of 87 gm. At this temperature, and much below, all virulence is destroyed. In the case of an adult male undergoing treatment at the Institut Pasteur paralysis supervened and became general, notwithstanding which the treatment was continued without interruption and the patient recovered. Another case of like character has occurred. These are all the cases of this nature in over 19,000 cases treated during twelve years, from 1886 to 1897 inclusive.

To the idea that this paralysis was a result of the treatment was opposed the small number of cases in which it occurred. Neurasthenia (hysteria) was suggested, also the action of some toxin other than that of rabies. Again, it was suggested that the paralysis was paralytic rabies caused by the bite and not by the treatment, which latter being administered without intermission cured the disease.

Suzor quotes from Gamaleïa the assertion that the virus can only spread from the periphery or external surface to the centre by the nerves. The physician ought to cease aiding the action of the virus by morphine; he ought to help the nervous system. Artificial respiration and strychnine are advised. Rabies is not so common in man as in the dog and the symptoms are not so severe. In the dog cases of undoubted recovery are on record, but the diagnosis in all cases must be a matter of doubt until proven by inoculative experiments.

Chloral and curare fail to cure; chloroform, or hydrobromate of hyoscine may be used palliatively. An intelligent citizen wrote me: "Do not let the boys one after another die of rabies; give them the brains of rabid rabbits to eat." In such an emergency *de gustibus non disputandum est.* In the light of modern therapeutics this suggestion in the abstract is not so absurd as it seems on first thought.

Preventive Treatment.

The death-rate in cases that have been cauterized is thirty per cent., in those uncauterized it is eighty per cent. Efficient cauterization is by the hot iron, thermocautery, sulphuric, nitric, or carbolic acid, chloride of antimony, or acid nitrate of mercury, applied in less than one hour after the bite. Sometimes it is necessary to open up wounds by incision, or even to resort to amputation. Otherwise the wounds are treated as are other infections. Sucking the wound, dry-cupping, and ligation of the limb above the wound may under some circumstances be useful preliminaries. But the physician must exercise judgment. The wounds may be so numerous, so lacerated, so sinuous, that it is impossible to cover the whole surface with the actual or potential cautery. Careful washing and syringing with antiseptic solution and the application of water as hot as can be borne (130° F.) are painful but can be endured. This application of hot water can usefully be made a part of the daily toilet for several months, say three months. Hot bathing, dry or moist air, persisted in throughout the incubative period, are useful adjuvants. Experiments seem to show that enfeebling excesses, especially alcoholic, increase the risk; the latter, some experiments seem to indicate, interferes with the measures for immunization.

What classes of bite shall be subjected to the immunization treatment? All in which the skin, the epidermis, has been abraded or scratched off by the teeth of the animal. Cases in which the skin has been merely bruised through untorn clothing may be exempt. Whenever and however the saliva, the secretions, or the tissues of rabid animals have been applied to denuded surfaces there is then risk, though it may be slight. Suspected animals that have bitten other animals should not be killed if they can be kept securely. If rabid they will probably die in two weeks, if sick of other diseases they may recover, if vicious they remain well. Should they die their bodies must be subjected to gross and microscopic examination: the latter may be restricted to the medulla oblongata, which should be inoculated into rabbits or guinea-pigs, preferably the former by trephining.

Immunizing prophylaxis may be produced by the Pasteur method in which the antitoxin is made in the body of the animal undergoing treatment. In the method of Babes, of Bucharest, the serum of an immunized dog is used. Tizzoni and Cantanni of Italy use the serum of immunized sheep. In this the antitoxin is formed in another animal and injected into the animal undergoing treatment. The animals immunized with the object of obtaining an antitoxin are not so rendered by the Pasteur method, but by means of a virus attenuated by peptic digestion. Some use a mixed method, partly indirect serum therapy and partly direct serum therapy. The following is the method of immunization practised at the Pasteur Department of the College of Physicians and Surgeons, Baltimore, Md., and it is identical with that of the Institut Pasteur, Paris.

Select a rabbit that has died of rabies after six days' incubation, having been inoculated subdurally by trephining and injecting, as has been above described. The rabbit must not be killed; it must be permitted to die, and its medulla oblongata must be extracted and used before decomposition has set in. Lay this rabbit on its belly on a zinc tray (79 cm. long, 54 cm. wide, and the border turned up 2½ cm.); make a cut with a knife or scissors from the nose upwards and backwards along the middle of the head and back to the tail, lay off the skin from the head and from the body down to the tray. With the scissors or knife cut off the muscles in long strips and lay bare the spinal lamina; cut off the spinous processes with scissors. Then thrust the beak of a Liston bone forceps into the orbit, cut the calvarium obliquely backwards; do this on both sides and unite the incisions by a transverse cut behind and in front. The calvarium may then be lifted off, or it may be removed bit by bit as the operator pleases. All the while the muzzle of the rabbit is held in Farabeuf's

notched forceps (the instruments are not devised specially for this work; they may be obtained from Collin, Paris, or skilled instrument makers everywhere). When the brain and medulla oblongata have been exposed, slit the dura and remove them, and place them in a sterilized saucer, base upwards. Cut the vertebral lamina on both sides with the bone forceps from above downwards; be careful not to tear the membranes or the cord. It requires practice to lay bare and extract the cord intact, particularly from the narrower parts in the neck and shoulders. Expose the cord for ten inches, divide it transversely at the lower end, seize the cord and the membrane with a pair of dissecting forceps (toothed), raise it, and cut from below upwards towards the head the spinal nerves which hold it. It may be placed in a sterilized dish or allowed to remain loose in the canal; cut two pieces each three inches long and tie a piece of sterilized thread to one end of each piece; withdraw the cotton stopper from the sterilized bottle, and put the piece of cord into the bottle without touching its sides; then put back the stopper which presses and holds the cord, a part of which is allowed to hang outside. Do the same with the other piece. Put the date on the label of the bottle and also the number of the passage, and also, maybe, the number of the rabbit that has undergone this passage—*e.g.*:

500–3.	500–3.
June 23d, 1898, 2 P.M.	June 23d, 1898, 2 P.M.
A.	B. × .

These bottles are duplicates, and they are immediately placed one behind the other on the shelf in the cord room, which is kept between 20° and 25° C. Should a culture from the cord exhibit a growth, a cross × is placed on the label; if it be necessary to use this cord it is reëxamined, and often the growth has disappeared. As a rule these growths are non-pathogenic, and cause no trouble when injected; occasionally the green pus organism is present. Such cords are rejected unconditionally, though this organism is itself non-pathogenic. After the cord has remained twenty-four hours in the cord room, a piece is cut off and dropped into bouillon in a test tube, which is put in a thermostat and examined after twenty-four hours. The bottom of these bottles is covered about 2 cm. deep with flake caustic potash, the piece of cord hangs over this, its lower end level with about the middle of the bottle. The glass manufacturers list these bottles as aspiration or irrigation bottles. Their capacity is one litre, they are 23 cm. high, 8 cm. in diameter across the bottom; on the side near the bottom is a nozzle opening into the bottle, and the opening has a diameter of 2 cm. The opening in the neck of the bottle has a diameter of 2½ cm. The open-

ings are plugged with cotton and the whole is sterilized in the hot-air sterilizer.

A convenient cord room may be constructed as follows: Partition off the corner of a room for a space of twelve or fifteen square feet; let the partition be double with a space between, which is lined with thick paper or asbestos. The room should have a window and a door; the latter and the shutters of the former are constructed like the partition; the ventilation should be through the roof. Two shelves run the length of room on one side, the first row, 128 cm. from the floor, is 42 cm. wide; forty-one inches above this shelf runs a similar one. A gas burner and two intermediate burners occupy one side of the room. The bottles with the cords are placed one behind the other on the lower shelf, fifteen bottles in front and fifteen bottles behind. This room is kept dark, with door and shutters closed, and only artificial light is used for illumination; in winter it is warmed with a Bunsen or a gas stove with thermo-regulator. The latter is not easily managed, however, and personal attention can sufficiently regulate the flame. The heat above mentioned is sufficient for this climate, in which a temperature of zero Fahrenheit is very rare. If the main room—that which includes the partition—be heated (steam heat), it is advantageous. The summer in this climate does not long remain at 90° F., but when about 84° some refrigeration will be necessary in the cord room. This may be simply accomplished with a mixture of the following proportions: Chloride of sodium (rock salt), 150 lbs.; sulphate of sodium (Glauber's salt), 50 lbs.; carbonate of sodium, 17 lbs. This is put with intervening layers of broken ice in a tank made of a galvanized iron cylinder with a bottom and a removable lid, 47 cm. high, 46 cm. in diameter. In the centre of this runs an open cylinder 11 cm. in diameter through the top and bottom; the bottom of the main cylinder is about 2½ cm. above the ground; the rim of the body of the cylinder which rests upon the ground is perforated with orifices 2 cm. in diameter and 8 cm. apart so that air may have access to the outside surface of the bottom. Fill the main cylinder with layers of ice and the above mixture, the first layer being ice. A small open nozzle enters the main cylinder at the bottom and is closed with a cork. The cylinder is put in a wooden wash tub and surrounded with sponges. This is placed in the cord room. Moisture of the air, which is undesirable, is obviated by chloride of calcium, in ordinary pie pans (tinned iron), which, to guard against leakage, are set in stoneware bowls. The room is not frequented; those only enter it habitually who must. It is furnished with a thermometer, registering maximum and minimum. When the floor is swept—which is rarely—wet sawdust is used, and the woodwork is washed in alcohol.

In starting a supply of rabbits and cords, trephine two rabbits daily for two weeks, keeping the cord that is being used in the ice-chest, in a sterilized test tube; in about two weeks the rabbits will begin to die daily, and ever after the supply must be maintained by trephining two rabbits daily. Thirteen boxes with twenty-six rabbits will be required for this alone; but twenty-five boxes will barely meet the exigencies of outside experiments in determining whether animals sent for examination are rabid. The rabbits are fed on a mixture of corn 1 part, oats 1 part, and bran 2 parts, with a little cabbage daily.

In preparing the emulsion with which to inject patients it is better to use the main room, and have a table with a drawer in which are labels, glass rods, curved scissors, and forceps, the glass rods having been wrapped in paper and sterilized in hot air. Erlenmeyer flasks, 100 c.c. capacity with cotton plug, contain water sterilized in the autoclave. There are also stout wineglasses covered with paper caps and sterilized in hot air; the wineglass inside does not taper to a point but has a flat bottom ½ cm. in diameter, which corresponds to the diameter of the glass rods which are 25 cm. long; the wineglass brimful holds 40 c.c. There is, of course, a Bunsen burner on the table. For the newly arrived patient the cord of the thirteenth to fourteenth day is used; that is, a cord that has been drying over caustic potash for thirteen to fourteen days. Such a cord measures transversely ½ cm. The cord is for one instant passed into the Bunsen flame, then with curved scissors, previously heated to redness in the flame and allowed to cool, less than a millimetre is transversely cut from the end of the cord and allowed to drop into the wineglass; ten such pieces measure 8 mm. and weigh 20 mgm. This is triturated with the glass rod until it has become thoroughly broken or mashed according as it is recent or old. Then a few drops of water are added and it is triturated until a milky fluid results, then more water is added until finally 15 c.c. is reached. The emulsion now looks like rice water and a sediment soon accumulates; the paper cap is put back on the wineglass and on the bottom rim, upper surface, is put a label with the number 14 on it, meaning a cord that has dried fourteen days (older cords, fifteen-day cords, are thrown out and the bottle is cleaned). The caustic potash after being twice used requires renewal; in twenty-eight days it looks like wet white candy. The glass rods wear smooth and require to have pieces cut with a file and broken off, thus becoming sharp again. The thirteenth-day cord is prepared in a similar way in a wineglass. These wineglasses are put in an agate-ware tray or baking pan in which are placed pieces of filter paper, and a bowl with some three-per-cent. solution of carbolic acid and two Pravaz syringes. A list is made out with the names of the pa-

tients and the ages of the cords (that is, the number of days the latter have been drying), and the dose, *e.g.*:

FOR JUNE 24TH, 1898.

	Cord.	Date.	Dose.
George Williams	10 days.	June 14th.	3 c.c.
Edward Cook	5 days.	June 19th.	2 c.c.

These lists are made out and put on the table the day before the treatment is begun, and are entered in the case book, which records the circumstances of the patient's case, *e.g.*, name; age; seat of bite; number of bites; animal that inflicted bites; cauterized or not; what has become of animal, etc.

The temperature of the cord room and of the outside atmosphere, and the result of the culture are recorded in a book on the table in main room. We now take the tray and go to the patient. The latter is permitted to stand, sit, or lie down as he or she may desire. The Pravaz syringes and needles, which have been filled with three-per-cent. carbolic acid solution, are emptied and washed out with sterilized water. These syringes, holding 3 c.c., are filled by thrusting a needle through the paper cap of the wineglass; then the abdominal region of the patient is bared and the site of the injection, hypochondria or anywhere on the abdomen, avoiding large veins, is wiped with filter paper wet with three-per-cent. carbolic-acid solution. Then the skin is raised in a fold between the fingers, and the needle is thrust well into the subcutaneous cellular tissue. It is important to avoid injecting the layers of the skin, which is painful, and to avoid the sites of previous injections. After the injection a piece of filter paper wet with the carbolic acid solution is put on the skin and allowed to remain for a few seconds.

We have not modified the dose relative to age. In our youngest patient, a girl two and a half years old, and in a lady aged eighty-four years, the same doses were given. At times there are redness and induration in the connective tissue, but there has never been pus, never cellulitis of the slightest gravity. Hot-water applications on towels suffice to remove these trivial inconveniences. The treatment occupies twenty-one days at least.

First day (thirteenth to fourteenth day cord) 3 c.c. at one time, and so on until the sixth-day cord is reached on the fifth day; two injections of the sixth-day cord emulsion are given in doses of 2 c.c., each at the same time; subsequent injections are: sixth day (fifth-day cord), 2 c.c; seventh day (fourth-day cord), 2 c.c.; eighth day (third-day cord), 1½ c.c. The injections are not given of cords earlier than the third day. Now begin again with fifth-day cord and come down to third-day cord inclusive; these all now being 2 c.c. doses.

If it be thought desirable to approach at first the more virulent cords gradually, when the fifth-day cord is reached, a fifth-day cord may be given again as the next day's injection; so also with the fourth-day cord, but after this the injections resume their regular course—fifth-day cord, fourth-day cord, third-day cord, and over again until the twenty-one days have passed, the dose being 2 c.c. each time.

Whether by a coincidence or not, the patients that I have observed—forty-six in number—have markedly improved in general bodily condition during treatment.

It is much to be regretted that a reliable antitoxin is not available to displace the foregoing elaborate technique. Until such shall appear, a close imitation of the technique of the Institut Pasteur, Paris, is the only way to be saved.

That purging, sweating, hot baths (water, dry air, or vapor), can eradicate rabies once it has reached the citadel of vitality, the medulla oblongata, is incredible, because it lacks experimental demonstration. That dogs, rabbits, chickens, and mice have recovered—the two former from the early stages prior to the development of acute symptoms, and the two latter even from advanced rabies with fully developed nervous symptoms—there can be no doubt, because these have been the subjects of experimental demonstration.

Effect of Heat on Rabies.

How do these animals sometimes—for it is very exceptionally—recover from rabies? They heat the virus out. The hen has a normal cloacal temperature of 108° F. From the moment the virus is inoculated she begins to attenuate it; this is proved by the long incubation, even with fixed virus amounting in some cases to over twenty or thirty days. Notwithstanding all these advantages the hen rarely fails to take the disease and rarely recovers, but she dies game, and the foe has likewise perished, the virus is sterile, the medulla is inert. As we noted above in the account of the experiment of Dr. Byron, medullas in an incubator for eight days at 40° C. (only 104° F.) gave marked rabies to rabbits, but the animals got well. At 50° C. (112° F.), these medullas produced no disease. At 108° F. the rabic virus in vitro becomes sterile; at 108° F. in the hen the rabic virus becomes sterile, but too late to prevent rabies, though it is so attenuated as to enable her sometimes to recover. Can the temperature of the human animal be raised in the medulla oblongata to 108° F. and maintained there for eight days? Or can it be raised to 108° F. daily and maintained at that point for a short time safely? To say the least, it is a dangerous temperature for the medulla oblongata of man. To put the *sine qua non* at its lowest terms, can a temperature of 104° F.

be obtained daily for eight days? Can it be maintained for eight days? Let the question of maintenance be abandoned as not feasible. Can a temperature of 104° F. be attained in the human animal once a day for eight days? This is giving odds against a negative result of the experiments, for in Byron's experiment 104° F. was maintained for eight days. The following experiment is not so thorough or conclusive as is desirable, but it elucidates some points regarding the effect of hot, dry air on rabbits trephined with rabies.

In taking the temperature the thermometer must be all its length in the bowel, only enough for holding remaining outside; with the ordinary clinical thermometer this can readily be done even in the guinea-pig. When in the hot-air room the whole thermometer must be within the sphincter ani, otherwise the temperature of the room would affect it. To do this, have a metal-case thermometer and tie a piece of thread around it so that the latter hangs outside the anus; take the temperature before putting the rabbit in the hot room, then return the thermometer to its case and gently push the whole instrument up the bowel and inside the sphincter, retain it by a compress over the anus and a tailed bandage. When man is the subject the procedure is the same, except that no means of retention are necessary.

Imprimis, it is necessary to know the relation of temperature in the medulla oblongata to that in the rectum. The results of some experiments which I have made show that the temperatures in the two places are the same.

A control rabbit was in the same room, the same basket, and subjected to the same temperature (not inoculated).

May 13th: Rabbit A in 175° F. for ten minutes. Temperature before, 102° F.; after (thermometer in case in rectum), 110° F.—all its graduation. May 14th: Rabbit A in 175° F. for twelve minutes; tremulous when it returned, 11 A.M. Found dead, 3 P.M.

Two rabbits were trephined from medulla oblongata of A. One developed typical rabies in six days and died of it. The other escaped. The virus in the medulla oblongata of A was not sterilized or attenuated by temperatures of 106° F. and 110° F. The mercury rose to what undoubtedly would have been registered 111° F. if the thermometer had been graduated to record it. The medulla oblongata of A was virulent on the sixth day.

Other similar improvements demonstrated that an average temperature of 104° F. in the medulla oblongata begun twenty-two hours after inoculation and daily repeated for twelve days, failed to sterilize or attenuate the virus in the medulla oblongata of the living animal (rabbit).

A vigorous man, aged twenty-four years, weight one hundred and

forty pounds, with the thermometer in the case and placed well in the rectum within the anus, subjected himself to a temperature of 162° F. dry air for fifteen minutes. The rectal temperature before, was 98.4° F.; after, 101.2° F.

At another time he was subjected to a temperature of 180° F. for five minutes; before, his rectal temperature was 98.4° F.; after, 106.2° F. Cold douche and cold-water swimming in thirty minutes reduced the temperature to 98.2° F. While subject to 180° F. dry air, he became dizzy, and "things looked blue."

Is it possible to maintain a temperature of 104° F. in the human medulla oblongata for eight days? And if so, would it cure or prevent rabies? We have answered the second part of this question negatively. With a temperature of 108° F. it does attenuate, and finally sterilizes the virus, but too late to prevent the disease. To all this, however, it may be objected that inoculation subdurally at once imparts the virus to the nervous system, and that bites as they occur in nature should be more closely imitated, *e.g.*, by hypodermic injection of virus. But in making this experiment, its frequent failure to cause the disease must be taken into account.

The writer makes no claim to originality in this paper, except in the sections on septicæmia, rabies in the mouse, Baltimore cases, and others, and in the experiment relating to the effect of heat, in the conduct of which he acknowledges his obligation to Mr. Melcher Ekstromer; and to Mr. Philip S. Chancellor for translations.

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PYÆMIA AND SEPTICÆMIA.

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PYÆMIA AND SEPTICÆMIA.

Definition.—The general term, blood poisoning, has been applied to a great variety of contaminations of the organism; while pyæmia is regarded as the result of the absorption of pus into the vascular system, septicæmia implies infection from different sources.

The septic process in pyæmia and septicæmia is very different from that in the acute disorders, such as diphtheria, malignant pustule, glanders, etc., or the more chronic forms of disease, such as scrofula, leprosy, syphilis, and the like.

Introduction.

This paper must necessarily be somewhat of a medico-chirurgical character, and yet in many of its phases may be purely medical. The line of distinction between surgery and medicine has been generally recognized as external and internal, but this does not give so good an idea of the difference as a division into organic and functional disorders. A mere temporary engorgement of structures which is not accompanied or followed by radical changes in the organization of the tissues and which is amenable to the action of drugs comes properly under the care of the physician. But a modification of structure as to size, shape, or density, whether internal or external, belongs to the domain of the surgeon.

When, however, this alteration of form is amenable to internal measures of treatment or yields to local external applications, without the use of instruments or operative interference, it has generally been regarded as pertaining to the practice of medicine. It may be said that in any inflammatory condition, where resolution is effected by medication, the case appropriately is included in the work of the physician, provided it is an idiopathic state. But if inflammatory developments result from traumatism, they are surgical, and whatever means of treatment may be requisite for their relief comes properly into the field of surgery.

Incisions and mechanical appliances of whatever kind do not limit the sphere of the surgeon to mere operative work, but he must resort to medication likewise in the preparation of his patient for an opera-

tion and in the after-treatment of his patient. Drugs become then the tools of the surgeon, and their influence is essential to secure the best results. Even the ordinary hypodermic injection of morphine and atropine, or the inhalation of chloroform, may be regarded as a surgical measure.

Before entering upon the consideration of the different phases of pyæmia and septicæmia, it may be stated that various effects ensue from what is commonly understood as blood poisoning. There are marked differences in the nature of the impression as well as in degree or intensity. Whether this is due to the character of the contaminating element or to the susceptibility of the subject is not always clear, but it is evident that one individual is more liable to suffer in this way than another, owing to some peculiarity of physical constitution. Again, the same subject may be attacked with a comparatively slight disorder at one time and a grave form on another occasion, according to the state of the secretions and absorbents at different periods, in connection doubtless with the greater or less virulence of the infecting element.

The operator may be contaminated by bringing his hands in contact with tissues in a state of decomposition at different stages of their disorganization and suffer accordingly with a more or less intense poisoning. But the most serious form of contamination results from wounds received in the performance of post-mortem examinations upon subjects dead of malignant disease, or from abrasions of the cuticle which may have escaped observation previously.

Precautions of various kinds have been adopted against such accidents, but the use of light rubber gloves is now generally employed in such work with exemption from any chance of absorption of vitiated matter. In the absence of these, coating the hands with carbolized vaseline is the best precaution we have discovered, and it is found effective also in protecting one while examining syphilitic ulcers by palpation.

In the other aspect of prophylaxis, surgeons have used white cotton gloves to prevent any possible contamination of the wound by septic matter from the hands in performing operations upon sound structures, and thus to prevent pyæmia and septicæmia in the patients. It behooves operators to adopt all those measures which are calculated to protect themselves and their patients, and the failure to do so has brought great trouble in the development of preventable disorders. We have somewhat frequently observed the effects of purulent absorption and septic contamination in the person of colleagues, resulting from lack of proper precautions in performing operations or in making post-mortem examinations; and some have been the subject of

repeated attacks of blood poisoning in consequence either of want of care or of an abnormal susceptibility to septic contamination.

It so turns out that notices of the slighter cases do not appear in print, but the knowledge of a considerable number of cases of this class satisfies us that they are of frequent occurrence.

All the practical applications of surgery may be appropriately classed under the headings of "Aseptic, Antiseptic, and Septic Procedures." The first embodies all those means which come under the head of prophylaxis, and looks to the avoidance of hurtful agencies, the operator thus being assured that if a measure does no good it will do no harm. It is the highest type of conservatism to preserve the organs or tissues involved in an operation against any sort of mutilation or injurious impression from other sources. The procedure therefore which affords the best guaranty against detriment to the structure of a part subjected to surgical treatment commends itself to adoption by the practitioner under all the varied surroundings of the case. From whatever cause impairment or disability of the constituent elements of a part may ensue, whether in the action of a disease upon its tissues, or from the operation which may be undertaken, with the concomitant dressings, it should be put to the account of conservative surgery.

Asepsis, as the derivation of the word implies, consists in opposing all contaminations from within and without a wound, and presupposes the vitality of the structures involved in the lesion, so that a part deprived of the supply of nerves and blood-vessels is *ex necessitate rei* beyond the sphere of curative agencies, and its loss is a foregone conclusion. It is therefore good surgery to amputate such a member at the earliest practicable moment after the infliction of a destructive injury.

Barring this class, the most extensive traumatism may be amenable to proper diligence in the application of aseptic measures, and among them cleanliness is of prime importance. The idea conveyed by freedom from dirt or filth applies not alone to the absence of any foul extraneous matter from the wound, but its complete removal from the surroundings and the bedding of a patient as well as the apartment. There are many cases in which medication is not requisite, and after the coaptation of the tissues by suture or otherwise, a simple cotton dressing with a bandage suffices for the cure.

A fresh incised wound, either from accident or in the course of surgical operations, having the minute vascular supply in a favorable condition to secure union by adhesive inflammation between the approximated parts, requires only to be clean and free from coagula to heal without the interposition of medication. But there is sufficient

evidence from the practice of those who have employed a simple solution of chloride of sodium for washing out the abdominal cavity, to rely upon its efficiency in such cases, and it is evidently innocuous; and it has been often resorted to for intravenous injections in cases of great vital depression from hemorrhage or other causes, with marked good results.

The possibility of leaving any portion of the fluid used as a wash in the abdominal cavity, and thus leading to its absorption, gives the chloride-of-sodium solution a decided preference over a carbolic solution, as the latter is liable to induce troubles of a nature which do not occur from the absorption of the former. The safest is therefore the best for general use.

This brings us to the consideration of antiseptic applications in surgery, which differ widely from aseptic measures in their aim and results.

The indications for this class of remedies, being founded upon the anticipation or the existence of septic phenomena, lead some to a recognition of the microbic origin of such troubles, while others hold that the developments are attributable to other causes. The truth, no doubt, lies in avoiding the extremes on either side; and for practical purposes it is not requisite to decide as to the etiological factor in the septic process. It is a gratifying reflection for the medical philosopher and scientist to point out the separate germs of the various disintegrating processes involved in the aggravation of wounds, and to define the special microbe of distinct diseases, but the practitioner is not always prepared to accompany the bacteriologist in such investigations, nor does it devolve upon him to accept the conclusions from his investigations for the application of remedies in surgical cases.

After a somewhat careful research of what has been accomplished by the microscope in detecting the different forms of micrococci, spirilla, spores, etc., and noting the discrepancy between the observations of different experts in this department, we are still in doubt as to the rôle of bacteria in causing the degeneration of vital structures. That such microorganisms with fungi and ptomaïns have a share in their development is evident, but whether the manifestations connected with their presence are *post hoc* or *propter hoc* has not been proven conclusively by the results of treatment. We know full well that this qualified incredulity will appear to those who are following in the wake of recent investigations as over-cautious, but while questioning some of the tenets of this new faith, our practice conforms in the main to that of its apostles, and we hope to be able to give a reason for our departure from their procedures wherever it appears that the latter may be hurtful to the patient.

To speak plainly, we are not following the dictation of any high-priest in bacteriology, but exercise the right of private judgment in this as in all other matters involving professional observation and research. Having the courage of our conviction based upon the investigation of this subject, we protest against a blind acquiescence in any and everything which may be styled antiseptic surgery, because it is backed up by respectable authority. There is much connected with the general observance of its doctrines which is commendable, and yet there are matters of detail which are superfluous and in some instances positively injurious to the patient.

In its essence antisepsis really consists in correcting a tendency to or a development of degeneration and disintegration of living structures resulting from contamination in any form. If we are able to discern the causative element and neutralize it by antiseptic measures of a constitutional or topical nature, this is of course the most rational procedure. But in the event of failure to identify the etiological factor, it then devolves upon the surgeon to combat the injurious effects of the vicious impression already made upon the organism, and this is by far the most important province of antiseptic surgery. All that is done in anticipation of trouble belongs to the domain of asepsis, and yet the claim for antisepsis includes many measures, supposed to be preventive of disorders, which actually become sources of disturbance, so that instead of protecting the organization, they produce derangement and lead to septic developments. This class of agents comes under the division of septic surgery. It is now well known that the imprudent use of carbolic acid locally has been followed by its absorption and a consequent derangement of the renal function. In like manner the employment of carbolic-acid spray has proved so detrimental not only to the patient but to the physician or surgeon, by inhalation of its noxious vapors, as to lead to its abandonment by most operators.

The evils growing out of the abuse of bichloride of mercury as a germicide are now so well known to the profession generally throughout the length and breadth of the medical world that we need not specify instances to any reader of current literature.

The profession has been advised recently of the infection of two prominent American surgeons in the performance of their work, and while they have escaped any serious results by timely treatment, both of them have suffered so as to render it necessary to suspend their duties for a considerable period. I wrote to these gentlemen for personal statements of their cases, and present them here with a view to caution others and to record typical cases of a disease that is confined generally to our ranks.

Dr. Roswell Park, of Buffalo, N. Y., writes under date of February 13th, 1898: "For eight months, and until the first of the year, I was completely out of work as the result of an infection. Now I am happy to report myself as well again and hard at work. My case has puzzled every one to whom it has been submitted, and no one term or even sentence would define it all. It certainly was a mixed infection, but just when it occurred I do not know. It came on slowly, with manifestations mostly confined to the lymphatics of the left arm and axilla. For two months these were troublesome. Then a sudden attack of a diaphragmatic pleurisy with probable mediastinal infection prostrated me. Then a few weeks later I had the lymphatics of the arm all dissected out. I was just getting out after this, when acute septic symptoms appeared and the axillary nodes swelled enormously. Then I had the axilla all cleaned out. Within two hours my temperature fell eight degrees Fahrenheit. But there was no pus present either time, and cultures and all sorts of bacteriological studies gave *no* result. After this I went to the seashore, came back with partial laryngeal (toxic) paralysis, went abroad, was quite sick over there, but finally came home quite well in every respect, only wearing my scars."

Dr. W. W. Keen, of Philadelphia, gives an account dated February 11th, 1898: "I made a post-mortem on a case of suppurative peritonitis following cancer of the stomach at 11 A.M., on January 9th, 1898. In doing so I inadvertently and very slightly pricked my right thumb with a needle. The hand was disinfected by washing, but the wound was so slight that it was not deemed necessary to lay it open at once. At six o'clock that evening I began to feel chilly; by nine o'clock I went to bed as I felt so unwell. It was impossible for me to sleep, because by that time the thumb had become the seat of severe throbbing pain and in the neighborhood of the prick the tissues were already becoming hard. By 2 A.M., feeling quite sure there was an infection, I called a brother surgeon who laid open the thumb and disinfected it with bichloride of mercury solution, 1:500, and applied the same as a dressing. A quarter of a grain of morphine gave some sleep, but by eight o'clock the next morning, about twenty-one hours after the infection, I was vomiting repeatedly and had a temperature of 105°. Twenty-two grains of quinine and six ounces of whiskey were administered in each twenty-four hours for three days with sufficient morphine to procure sleep. The pain was very severe. The swelling of the thumb was so great that all the tissues were under great tension, so that it was feared that either necrosis of the last phalanx would take place, or as a dark spot appeared on the edge of the wound, that possibly gangrene of the tissues

might follow. Accordingly on the third day the incision already made was enlarged and the parts were disinfected anew. Fortunately, the lymphatics were never involved. Within ten days the constitutional symptoms had disappeared, but the thumb did not heal for about six weeks. Two cultures were taken from the incision in my thumb (of course after the primary disinfection), but showed no growth whatever, though taken separately on different occasions. Unfortunately no culture was taken from the abdomen of the patient at the time of the post-mortem, so that I do not know what the nature of the infection was. It seems to me that the very prompt incision made by Dr. Taylor and the thorough disinfection account for the absence of lymphatic involvement, for I never had the slightest tenderness in the axilla; and they also account for the sterile cultures."

Dr. Lewis Wheat, of Richmond, Va., was not so fortunate as Drs. Park and Keen, but much more fortunate than the average sufferer from septicæmia which has run its course. He writes March 24th, 1898: "While doing a very difficult and dirty perineal section for stricture of the urethra with multiple fistula, I injured my left index finger just at the matrix. This was on July 3d, 1884. The next day there was no local symptom, but I was feverish and uncomfortable. On the 5th I noticed decided inflammation with enlargement of the lymphatics. Twelve hours after, my whole hand and arm were terribly swollen, even the pectoral muscles were involved. The finger was treated by free incisions and constant immersion in a solution of chloral hydrate, five grains to one ounce of water. The swelling and pain in the arm and chest subsided in about one week, but gangrene of the finger took place and it was amputated by Dr. Hunter McGuire at the lower end of the metacarpal bone. Upon examination it was found that my great suffering was due to endostitis. The phalanges and metacarpal bones were all destroyed."

Dr. J. McF. Gaston, Jr., suffered from sapræmia, due to a wound from a tenaculum in a post-mortem operation done by him on a septic patient. He had a temperature of 103° lasting about twelve hours. A crucial incision was made in the palmar aspect of the second forefinger at the point of the puncture, between the first and second phalangeal junction, when the surface was cauterized by pure carbolic acid. Thorough purgation secured by repeated doses of calomel, and the use of a mixture of potassium chlorate, nux vomica, and cinchona led to recovery within three or four days.

In two other cases the infection was complicated with other diseases, and ended fatally. Dr. M. B., aged about forty-five, and a general practitioner in Savannah, Ga., suffered from pyæmia and septicæmia. The infection was from a needle left in a sponge which

Dr. B. was using during an operation for lacerated perineum. Lymphangitis and suppuration of the glands of the elbow and axilla followed. Pus was evacuated. Antistreptococcic serum was injected hypodermically, but unfortunately this was followed by eruption and bad results, the case ending fatally the next day after its use. The other case was one in which vaccination resulted in pyæmia and septicæmia complicated with typhoid fever, but was unusually severe. The caution as to the use of antistreptococcic serum given by the death of one of our prominent Georgia physicians leads us to agree with the statement of Louis Cobbert that the serum cannot be recommended for use in the treatment of human beings.

The two following were cases of great gravity, but with fortunate issue, occurring in members of the medical profession—one being in the person of an interne in the Providence Infirmary at Atlanta, and the other in that of a prominent practitioner of Anniston, Ala.

The former occurred from slight injuries to the hand in making a post-mortem examination, under the writer's observation, and came under his care. It began with points of local irritation, extending to the entire arm, and becoming in a few days a constitutional disorder. It ran through a most violent course, attended with suppuration at various points in the hand and arm, and leaving the subject extremely prostrated and emaciated, with a long, protracted convalescence. There was finally remaining only the stiffening of the two fingers of the affected hand.

The second case was seen in consultation. It occurred in consequence of a scratch by a piece of necrosed bone, in performing a surgical operation. Incisions had already been made to relieve tension at several points about the hand and wrist, and the patient was kept under the influence of morphine. It may be briefly stated that under appropriate treatment, he eventually recovered entirely.

A few typical cases occurring from other causes than direct infection in post-mortem examinations, and in people carrying on the ordinary avocations of life, may be instructive.

Dr. P. E. Murray, of Atlanta, stated in a private communication his experience with a fatal case of septicæmia resulting from an abscess of a tooth, which was treated by dentists, but was never extracted, as it should have been, in order to procure proper drainage for the peridental abscess.

The same physician treated a case of pyæmia resulting from a punctured wound in the forefinger which had come in contact with the fin of a dead fish. The inflammation of the soft parts was considerable, but the bone was uninjured. Pus formed and evacuated itself on both dorsal and palmar surfaces. The finger was thoroughly

cauterized with nitrate of silver and bandaged with adhesive strips. Calomel was administered and was followed later by trifolium compound and sarsaparilla. After more than sixty days' disturbance of his health complete recovery resulted. In the earlier conduct of this case another physician had injected carbolic-acid solution by means of a hypodermic needle into the tissues involved. The fault in this was in not opening by a crucial incision before the use of the carbolic acid.

A case of blood poisoning from the wound of a dead fish fin was also seen during the senior author's work at the Cotton States and International Exposition, where a great many fish were prepared for the visitors at a restaurant near the exposition hospital. The man's arm was very much swollen within a few hours after the injury. The patient was seized with rigors, faintness, nausea, and vomiting, and complained of headache and pain in the arm. His arm was very much swollen, red, and angry. The treatment instituted was to incise the point and to dress antiseptically with turpentine and olive oil and camphor. At the same time calomel and soda, followed by quinine and phenacetin and salol were administered. He was ordered to get a flaxseed poultice and apply every two hours warm. He was very sick for a day but gradually recovered. His temperature was at one time quite high, but after thorough purgation he was free from fever. Dr. P. E. Murray also treated a similar case successfully with turpentine and camphor after free incision.

It has been the senior writer's good fortune during a large experience in surgical work and in performing post-mortem operations to escape any constitutional contamination; he suffered only slightly on one occasion from local infection from dressing wounds several days after they were received on the field of battle. In view of the fact that several points presented festering sores on his hands from contact with wounds which were undergoing purulent degeneration from delay in receiving attention, it is inferred that the septic matter failed to produce blood poisoning because of not finding a state of susceptibility in the organization.

We may therefore look for an explanation of the greater tendency of some than of others, who undergo the same kind of exposure, to suffer from purulent infection in the underlying predisposition of the former and the comparative immunity of the latter to septic contamination. But the necessity of the exercise of all due precaution is accentuated by this condition of susceptibility.

Cases of infection from the tubes used by bacteriologists are frequent. The bacillus of tuberculosis has been known to be inoculated into the hand of the bacteriologist cut by a piece of broken test tube.

In the same way anthrax has been inoculated into the finger of a bacteriologist. Blood poisoning frequently results from a carbuncle. Septicæmia and pyæmia are results of human bites, of vaccination, abscesses in the accessory sinuses of the nose, criminal abortion, puerperal infection, wound from a dead fish's fins, nail wounds, abscess of the tooth, and many minor surgical operations. An abundance of caution in dealing with all of the above conditions is not overcarefulness.

In cases of puerperal infection we have a condition very closely allied to septicæmia. We also find toxæmia due to fecal impaction of long standing. Both of these conditions are complications which are often found after surgical operations. Recent reports of Gould and Colman of cases before the Clinical Society of London make this subject especially appropriate.

The case of Gould was one in which volvulus had existed and the operation was successful, but unfortunately the contents of the bowels were regurgitated into the stomach and were absorbed.

The case of Colman is interesting in view of its having been diagnosticated as intestinal toxæmia; the patient was treated successfully and was restored. All symptoms were relieved by enemata.

The existence of mania in this case makes it very similar to the one described by Hippocrates in Criton of Thasno, who stated that the patient was "delirious, deranged, furious," etc. In Gould's case an erythematous rash was only a symptom of septicæmia and coma showed the toxic effect upon the brain. The condition known as autointoxication exists frequently in typhoid fever and scarlet fever from intestinal absorption of ptomaïns in the fecal matter. In stab wounds and gunshot wounds perforating the intestines septicæmia of the same kind results from absorption and failure of elimination.

History.

Hippocrates, Galen, Maggi, Paré, and others have contributed valuable information on the subject of septic and purulent diseases. The literature dates back to a period before Christ when Hippocrates described a case of fever which could not have been caused by the ordinary condition of wounds even in his day and time. He calls attention to the rapidity of the progress of the disease and the final death of his patient in two days. It was a case of pure septicæmia without the complication of pyæmia or the intervention of sapræmia. The condition of the bowels, the coated and furred tongue, and the high tension of the blood-vessels are depicted in vivid terms, and the case is justly entitled to be classical and to come down to the twentieth cen-

tury as a typical case. The man's name was Criton, and he lived in Thasno. He was taken with violent pain in the great toe, and he was obliged to go to bed. The same day he had a rigor, suffered with nausea, and was delirious. On the second day swelling of the foot was noticed, and about the ankle there was erythema with distention and small bullæ. He had colliquative diarrhœa. The mania sometimes noticed in septicæmia is also mentioned as one of the symptoms of his disease.

Adams' translation of the works of Hippocrates gives the words of the Father of Medicine concerning this case and also others of puerperal fever, empyema, and other diseases in which septic processes gave rise to fever. His commentators and followers mention cases of traumatic fever with unusual intensity, and we owe our knowledge of these to Spigelius, Tacontius, and Celsus; Arætæus during the Christian era spoke of metastasis in cases of pneumonia. His views on abscesses of the liver betoken great study and close observation and are very much like those held at the present day. He regarded abscess of the liver as the result of intemperance and protracted disease, especially dysentery and colliquative diarrhœa. The name putrid fevers was given to many diseases described by Galen, Aetius, Synesius, Constantus Africanus, Alexander, and Palladus. Therefore the great ideas of putrefaction and of infection were brought out early, and the recognition of metastatic abscesses in the lungs or kidneys was shown by its mention by Arætæus.

The treatment of septicæmia and pyæmia was, however, very little understood before the time of Ambroise Paré. Maggi had also written a treatise on "Gunshot Wounds," but beyond the practice of pouring hot oil into the tract of a bullet, no treatment was advised. This was based upon an erroneous teaching that the bullet itself was poisonous.

In 1551, Paré taught the doctrine that infection came from external objects in gunshot wounds.

Vitiated air and the close proximity of decomposing vegetable and animal products were, he thought, the sources of this infection. A very interesting anecdote is told of his beginning the use of turpentine as an antiseptic in gunshot wounds. He had exhausted the supply of oil, which had been used at the boiling point, upon all the soldiers wounded in battle heretofore. Having quite a number to treat after a battle at Susa in 1536, he decided to use oil of turpentine and oil of roses as a dressing. He felt no great concern as to the outcome of those soldiers' wounds which had been burned out, but spent a sleepless night for fear infection might be carried to the whole system from the lack of oil to burn out the other soldiers' wounds.

But in the morning he found that more were complaining of pain and symptoms of septic fever among the former than among the latter. In fact, the turpentine served his purpose so well that he did not use the boiling oil any more. This was really a great advance and marks an epoch in conservative military and civil surgery.

Paré in 1582 taught that abscesses in the lungs and kidneys and other internal organs may arise from the state of the blood from wounds and changes in the composition of the air.

In 1553, Nicholas Massa also took this position. Valsalva and Dessault traced the origin of abscesses to injuries of the head, and there was quite a uniformity in the experience of surgeons that multiple abscesses were the results of wounds or injuries to the head.

Haller made the first experiments of any consequence on putrefying substances, in the eighteenth century, but Pringle had devoted a whole chapter to this subject in his book on "Bad Air," and many experiments to ascertain the value of antiseptics in the presence of putrefying substances are described by him in a crude manner. The most learned conclusions that were reached by Pringle did not go beyond the general notion that there were noxious gases, which were very volatile, and that these gases were products of decomposing straw, manure, and other organic substances.

John Hunter in 1793 demonstrated the presence of pus in the blood of patients who died of septicæmia.

Harvey's proof of the circulation of the blood gave an explanation for pyæmia, and Velpeau agreed with him subsequently as a result of his own experiments. Velpeau considered pyæmia a mixture of pus and blood.

In 1829, Cruveilhier seems to have formed the idea that pyæmia was a disease whose elimination by the emunctories is impossible and to have fallen into the error of believing it to be phlebitis. Gaspard and Ernst and R. Virchow showed by experiments that pyæmia was not phlebitis and not the product of the inflammation of the walls of the veins. They proved that thrombi formed in the veins and that this decomposing blood clot favored the formation of abscesses. They separated the two diseases, pyæmia and septicæmia, into two surgical affections of different character based upon the absorption of septic material.

Panum showed that the products of fermentation were not really volatile, but were stable, non-volatile chemical substances, and that the circulation of the blood was interfered with by these substances.

These observations of Panum cannot be too highly regarded, as they were made ten years previous to the time when Lister promulgated his views on antisepsis in 1865, and caused the world to look

for a fermentation as the cause of pyæmia and of septicæmia, and to explain the existence of pus.

Hemmer won a prize in 1866 for the best essay on the action of putrefying substances on the animal organism, and was awarded this honor by the faculty of medicine at Munich. His experiments were numerous and his conclusions quite as valuable and praiseworthy as those of Panum, who had priority in expressing similar views.

Pasteur had discovered germs or ferments in the air, and Alphonse Guérin in 1870 seized upon the plan of using cotton as a dressing, which is known now to absorb pus and to keep out infection.

Coze, Feltz, Belvier, Lionville, and Davaine, showed by experiments that germs did exist in the blood of animals into whose jugular vein pus had been previously injected.

In 1877, 1878, and 1879, Pasteur communicated to the Academy of Medicine the result of his investigations going to prove the presence of pyogenic bacteria, and also their rôle in pyæmia and septicæmia. Pasteur and Lister had both found these in the air, while Guérin had said: "So, said I, then, the miasms are the ferments. I am able to protect the wounded against their influence by filtering the air, as Pasteur had done, while maintaining in opposition to Pouchet of Rouen, that there is a spontaneous generation. I thought then of the cotton-wadding treatment, and had the satisfaction of seeing my anticipation realized. It was from this time that dates in reality the theory of germs or of ferments as a cause of purulent infection."

Etiology.

The staphylococcus pyogenes aureus is found in the pus in cases which run an acute course, and the staphylococcus pyogenes albus, or citreus, or pyocyaneus in pure culture has been found in abscesses from which there was evacuated a white, or greenish, or even black pus. A case of Wohlgemuth was a remarkably prolonged one of infection by the coccus albus. The case was clearly one of pyæmia developing multiple abscesses which appeared in various parts of the body. The final cure effected was after five years of treatment.

Other pyogenic cocci, as concomitants of these, are developed in the process of putrefaction going on around an ulcerated surface, and in the progress of the disorder known as pyæmia, and are to a great extent characteristic of the purulent process in the different structures. But these are not regarded as pathognomonic in the sense that the presence of a special bacillus is held to be indicative of the corresponding disease of the general system. The actual injection of pus into the circulation does not cause pyæmia proper.

The connection of pyæmia and septicæmia with microorganisms of various kinds does not lead to any definite recognition of a bacillus as the causative element, and we are warranted in attributing these disorders to ptomaïns or other putrefactive agents, independent of a distinct bacterial origin. Yet the distinct results obtained by anti-streptococcus serum and the constant presence of infusoria in the blood after injection or inoculation of putrid fluids both tend to cause the impression that the system is more susceptible to ptomaïns in the presence of living organisms than alone. The microscope revealed to Pasteur two vibrios as the chief producers of pus.

Morgagni has given us an idea which has since been found to be very well recognized in the beginning of this century by the elaborate elucidation of the subject by Duquesnay, and more recently by Roswell Park, and especially Ransohoff. The principle is that pyæmia often results from autointoxication or infection from within. The natural elimination of the products of combustion and of digestion, as well as the excretory processes, is not accomplished by the liver, lungs, bowels, and kidneys, and we have a depot of infection in these organs or in the system generally diffused.

Gangrene very frequently results in septicæmia. The system in such cases is poisoned by degrees. There are well-authenticated cases of the gradual poisoning of the system for two years after the first distinct impression of a toxic character. The symptoms of gangrene are therefore to be remembered and to be carefully watched. Pain is one of the first, a stinging, aching, benumbing pain, of neuritis. The most frequent accompaniment of the course of gangrene is diminished sensibility and a reduced temperature in the limb. In two marked cases of gangrene of the fingers septic processes had set in before amputation was performed. In another case in which Dr. J. McF. Gaston, Jr., performed an amputation of the leg at the point of election, or the tubercle of the tibia, no distinct septic infection had supervened, but a definite line of demarcation occurred before the operation was performed, while the line of union in the stump was complete within a week after the amputation. The other leg was to a great extent involved, due to necrosis of the first phalanx of the great toe. The free use of permanganate of potassium served to prevent further infection of a septic character in both limbs. The internal administration of Basham's mixture with chlorate of potassium served to eliminate the poison and to build up the system. The man recovered entirely and was able to work afterwards. After a year's time, however, the diseased condition of the femur, above the stump, gave rise to a local necrosis. The bone was thoroughly cleaned with permanganate of potassium, and large pieces of necrosed bone

were excised. The bone was restored and healthy granulations filled up the large cavity left after the excision. Septic contamination was prevented by prompt and thorough excision of the parts, and only after the arteries, veins, and lymphatics were in such a condition as to insure restoration above the point of removal.

Cumston, of Boston, says: "The pain is often sufficiently sharp to produce a restlessness, insomnia, and frequently there is delirium with fever; the patient presents extreme prostration, there is anorexia, a profuse diarrhœa occurs; fever declares itself, and the patient is quickly carried off by a true septicæmic process. All these symptoms are due without doubt to absorption within the economy of a part of the tissues and liquids from the focus of the gangrene, and the autotoxæmia is all the more serious because it occurs in elderly people having a generalized arterial sclerosis, and consequently whose kidneys are insufficient. . . . Septicæmia is the most dangerous as well as the most frequent complication, and as an illustration of this I would mention a case reported by Mendel of a man of sixty-seven years presenting a senile gangrene. The patient died of septicæmia in a few days, and the obliterating phlebitis in the tibial vein, the fluid condition of the blood, as well as the great softness of the spleen, left no doubt as to the anatomical diagnosis. . . . I would mention the fact that in these cases of septicæmia the liver and spleen show signs of an infectious process. In other cases, instead of a general infection occurring at once, a senile gangrene may produce a lymphangitis and abscesses."

Lilienthal draws attention to acute sepsis after ordinary urethral exploration with a soft catheter. Urethral chills were followed by septicæmia and death after internal urethrotomy. He also mentions other causes of pyæmia. One of the complications of the tension upon tissues formerly lacerated has been septicæmia. The stitches which were used in a flap-splitting operation for lacerated perineum gave rise to great pain, and when removed by the operator disclosed a large amount of pus. A fatal termination was then unavoidable.

In this connection it is important to emphasize the necessity of careful attention to minor injuries; for nothing of this kind is too trivial for the careful consideration of the conscientious practitioner. It is a matter of observation that many patients who present pyæmic symptoms after operation or injury are from various causes more or less debilitated, and for that reason a tonic course of treatment during the period of diseased action should not be neglected. Physicians and nurses who are especially exposed to wound infection should guard against abrasions and punctures so far as possible during the treatment of disease, and when operating upon all classes of patients

as well as when conducting post-mortem examinations (*Southern California Practitioner*).

Morbid Anatomy.

That pyæmia may occur independent of any ptomaïn element is a fair inference from the history of cases in which purulent absorption seems to account satisfactorily for the train of disorders observed. In the cases of multiple abscesses which are developed from a purulent focus, there is no reason to doubt that pus has entered the lymphatic system and, being arrested at certain points, leads to local collections of a purulent character. These abscesses conform in most respects to the characteristics of what is known as cold abscess, partaking of the nature of chronic abscesses; and they are rarely accompanied with the acute inflammatory manifestations of phlegmonous abscesses.

When a purulent focus leads to the absorption of pus there must be a deficient formation of that protecting sac known as the pyogenic membrane and, consequently, the purulent collection escapes into the connective tissue, and is taken up by the lymphatics and conveyed to the blood-vessels or the capillaries. It then becomes absorbed and, in some way not very well defined, develops pyæmia commonly understood as blood poisoning.

There may exist a local contamination from contact with septic matter, which spends its influence upon the part and forms a circumscribed abscess, without manifesting constitutional effects. Again there may occur absorption of pus through a slight prick or abrasion of the cuticle, attended with but little local irritation, which will lead to general disturbances of a grave character. The development of lymphangitis is marked by redness and tenderness along the tract of the lymphatics and by inflammation of the lymphatic glands.

This is accompanied with decided febrile reaction and prostration of the vital forces, and terminates either by resolution of the inflammatory process or by suppuration at different points from arrest of the lymph in the swollen ganglions. It sometimes appears to lessen and mitigate the constitutional disturbance when these local collections of pus are discharged by free incision and drainage. But on other occasions no relief is afforded by their evacuation, and other points become the seat of suppuration with an aggravation of the symptoms of purulent absorption and infiltration.

These collections of pus are not confined in distinct and circumscribed areas by pyogenic membranes, but permeate the cellular tissue and extend along the sheaths of the tendons, thus assuming the

character of diffused abscesses. The toxæmia may be limited to one side of the body entirely or may extend throughout the absorbents on both sides and thus become general, involving the whole system. The exhaustion of the vital forces at this stage is usually accompanied with great emaciation, and the nutritive process becomes so much impaired that nourishment avails but little. In a paper submitted to the American Surgical Association in 1893, the full report of a most protracted case of pyæmia was given in detail. The patient presented all the various features of the different stages of this affection, and we would refer those who are interested in the history of this disorder to the transactions of that year for information in regard to the progressive destructive work of this disease to its fatal termination after the lapse of nearly five months, attended with extreme emaciation.

Lymphangitis.— Inflammation of the lymphatics results from lesions of the minute ramifications of the branches of the absorbent system in the superficial parts of the body. While Hamilton and Gross have retained the term lymphatitis in their works on surgery, the word lymphangitis is adopted by Agnew, Smith, Treves, Keen, and Busey. Ashhurst designates this inflammatory condition of the lymphatic glands as angioleucitis. Bellamy, in his article for the "International Encyclopædia of Surgery," styles it lymphangitis, using the term tubular lymphangitis for inflammation of the larger continuous lymphatic trunks. Lymphadenitis indicates inflammation of the glands into which the affected lymphatics empty.

The etiological factor and the pathological changes resulting therefrom are involved in doubt, which even the advances in bacteriology have not cleared up satisfactorily. But it is well known that the slightest injury of the peripheral branches of the lymphatic system may be followed by the very gravest constitutional effects. Extensive traumatism of the vital structures rarely, if ever, induces lymphangitis. But a slight abrasion of the cutaneous tissue of a finger or toe may cause irritation which is extended along the lymphatics to the axillary or inguinal glands, and is attended with disturbances of the whole physical organization.

The correlation between the capillaries and the minute nerve fibrils in the affected part is evidently disturbed at the very outset, and the ganglionic element of this network of terminal branches being perverted, explains the derangement of the absorbents which ensue.

Sufficient importance has not been assigned to this triune organization of minute nerves, blood-vessels, and absorbents in attempting to fathom the depths of pathological diagnosis. There is such an intimate relation between the capillaries, the nerve fibrils, and the

lymphatics supplied to the skin that any irregular local impression upon a particular portion of the cutaneous investment of the body is soon communicated through the nerve centres to the internal viscera. A perverted action in one part is propagated to other parts so as to induce general disturbance of the system.

The constitutional derangement accompanies the external superficial inflammation, and fever with prostration of the vital forces indicates the pervading influence of the septic contamination. While lymphangitis originates frequently from slight superficial abrasion of the skin, it is held that some poisonous element enters through the lymphatics and involves the nerves and vascular system.

The cause of this affection, according to Rosenbach, is the invasion of the lymphatics by a specific thread-forming, spore-bearing microorganism derived from decomposing animal matter. It would seem that some modification of the inflammatory process, such as we have suggested for the incipient element of tetanus in a discussion on this subject before the International Medical Congress at Washington, may apply in this case.

The presence of a factor with the characteristic ptomaïn quality may account for the extension of a septic influence to the adjacent and more remote parts. In the former it produces results in certain areas of lymphatic radicles, and in the latter it involves the larger continuous lymphatic trunks, under the designation respectively of reticular and tubular lymphangitis. The difference between the ordinary results of an irritant and the special manifestation of lymphangitis depends then upon the ptomaïn element.

The development of traumatic neuritis is the most common complication of surgical cases; and there is rarely any extensive lesion which is not accompanied with more or less pain depending upon the inflammation of the nerve or its neurilemma. The irritation of the peripheral branch of a nerve may set up a train of disorders terminating in tetanus or lymphangitis, and the serious consequences of both these affections are well known. In the latter condition not only the lymphatic ducts become implicated but ganglions are involved in the inflammatory process, and suppuration is set up in the course of the lymphatics, with the characteristic features of pyæmia, terminating in multiple abscesses in various portions of the body.

The cutaneous development of the minute branches of the cerebro-spinal system of nerves and the ganglionic ramifications of the great sympathetic are so related to the capillaries as to establish a reciprocal action and reaction between them and the great nerve centres. The vasomotor nerves are so intimately linked with the excitomotor, the excitosecretory, and the excitodynamic system of nerves that

impressions made through the superficial afferent nerves are conveyed to all the corporeal structures and tissues so as to produce their effects upon the different organs. Reflex phenomena depend on a complex interchange of local pathological conditions through the nervous ramifications to remote parts of the body.

Observation of the changes resulting from inflammatory processes should be accompanied by a study of those modifications impressed upon the tissues by impairment or undue activity of the nerve element which enters into their composition. That many operators fail to take the nervous system into account in the management of their cases shows a lack of due consideration of the surroundings of a patient. A skilful operator may be disqualified for the highest attainment in surgery, through neglect of proper precaution in proceeding with an operation, or subsequently.

With our deficient knowledge of the etiological factor in that condition known as shock, I am inclined to the view that a continuous baleful influence is propagated to the nerve centres from the disintegration of the structures involved, and that this may be modified favorably by amputation with a clean incision through sound tissues above the point of injury, very soon after such violence to the parts. A proper appreciation of the participation of the ganglionic nervous system in shock should impress the great urgency of arresting the morbific influence by removing the cause.

The motor and sensory branches of the cerebrospinal system of nerves are so related to the ganglionic nerves that an impression is propagated from the former to the latter by every change resulting from violence. We are therefore prepared to expect surgical shock involving the organic nerve centres after any accident accompanied by great laceration and contusion of the soft parts, or after a comminuted fracture of the bones of the lower extremities.

To a greater or less extent the injury inflicted on the superficial cutaneous nerve fibrils is extended to the internal organs by the correlation of the nerves and capillaries with the viscera, and any extensive injury to the surface, however slight, is attended by marked vital depression. A striking illustration of this fact is presented in the grave effects of slight superficial burns extending over a large surface, and the serious consequences of the stings of wasps or bees over any considerable part of the body, though each is insignificant in itself. The notable effects observed after the application of cups, sinapisms, and blisters to the skin are likewise due to the sympathies established through this channel of the nerves.

An evidence of the mutual dependence of the superficial and deep-seated structures is furnished by the fact that, under some conditions

of the organism, an irritant fails to manifest its influence on the tissues. The mustard or cantharides may be applied to the surface for the ordinary period, under such a depressing modification of vitality, without producing any perceptible effect. Yet, when a change has been effected in the state of the organization, normal susceptibility is restored. The natural sensibility returns to the skin, and irritation, with the consequent inflammation, manifests itself in the parts where no effect was previously observed. A rigid investigation of the nerve element implicated in this condition is required by those who would fathom this lack of the excitodynamic function of the nerves.

Symptomatology.

The symptoms of the disease known as pyæmia are not always sufficiently characteristic to cause the presence of pus to be seriously suspected until the indubitable evidences of fluctuation, and the test by the hypodermic syringe reveal it. This has been the case more than once in our own experience. The temperature and the signs of decomposition of tissue may cause strong suspicion, yet the evidence of the aspirating needle is in some cases misleading. The needle may become clogged with a portion of the hepatic tissue in passing through the liver, and the point may really be in the pus and yet no evidence of the fact be present. The pus itself may be so thick as to make its passage through the bore of the needle impossible, and an incision into the tissue itself may be necessary to reveal the presence of pus. Again the abscess itself may be situated so deep and the tissues surrounding it may be so healthy in appearance that there may be nothing to indicate its presence. The tissues around a perineal abscess, an abscess of the appendix, or an abscess of the thigh may be healthy even in close proximity to the pus. In such cases a pyogenic membrane has formed around the inflammatory product, and has effectually stopped the progress of the cell destruction, while the germs also are inhibited and closed in, as it were. The pain may be considerable from the tension thus exerted upon the tissues. The pain should be a guide in performing an operation.

But the ramifications of the nerves are so that the pain is not to be found at the point of pus formation. The frequent difficulty in making a diagnosis may be illustrated by the following case which was reported by Dr. Gay. The patient was a physician, a man over six feet four inches in stature, and of magnificent proportions otherwise, who sustained a slight scratch, resulting in pyæmia. His finger was scratched and the red line indicating the tract of lymphatics extended to the arm-pit. This red line was narrow and was

discovered early. The chill which ushered in the septic infection was followed by high fever. The grave symptoms were not controlled by the remedies applied. An abscess extending from below the arm-pit to the hip was discovered and over a gallon of pus was evacuated. The infection came from some troublesome sores which he had dressed in one of his patients. The case ran for ten days before fever and pain subsided, and before consciousness returned. The delirium was indicative of involvement of the nervous centres, and so we may explain the complete paralysis of his body which was present.

A colored man, about 30 years of age, had enjoyed complete health until attacked with typhoid pneumonia some twenty months before coming under observation, after which he suffered from general prostration, terminating in the development of several tumors in the lumbar and femoral regions. Upon examination a large tumor was found extending from the left lumbar across to the hypochondriac region of the same side and reaching below the points of the false ribs; in this fluctuation was evident, but deep seated. There was no indication of pointing or thinning of the superficial tissues, but a general protuberance. An enlargement of the structures composing the posterior aspect of the left thigh immediately below the gluteal region, with evidence of fluctuation in a limited area, was also very perceptible, and materially interfered with locomotion. There were two other prominences near the sacrum, one of which could be traced towards the left iliac region. It was thought proper to make an exploratory puncture at the time in the left lumbar region; more than usual resistance was found after passing through the subcutaneous cellular tissue, but the instrument was finally thrust into a cavity, from which there flowed through the cannula pus of a character corresponding to that observed in scrofulous abscesses. With the recognized practice of avoiding a free opening in such cases, we employed the aspirator for drawing off the contents, but found that all the accumulation was not discharged, owing to the clogging of the tube. On the day following it was concluded to take the choice of evils, and make a free incision into the abscess, when again the operator was impressed with the dense nature of the investing tissue, and considerable force was required to penetrate the cavity with a sharp-pointed bistoury. A copious discharge of purulent fluid, mixed with cheesy flocculi, resulted from this free opening, and a tube eight inches in length was left in the cavity to effect thorough drainage, while a firm compress was secured by a bandage around the body.

We wish to impress the great importance, in these cases of extensive abscesses, of approximating the walls by compression at all points except immediately around the external opening, so as to agglutinate the surfaces of the pyogenic membrane. If all the pus of an abscess is evacuated, a vacuum is left, and there is a great proneness to redevelopment, unless such compression is resorted to

and kept up continuously, in order to favor union by granulation between the approximated walls. The presence of a pyogenic membrane in all abscesses serves to protect the adjacent tissues from contact with the pus, and without this provision purulent absorption would doubtless occur in most instances of suppuration.

The dense and resisting nature of the pyogenic membrane was a remarkable feature of this case. It was found that the discharge diminished in a few days, so as to render the drainage tube unnecessary, and, with the application of absorbent cotton over the opening, and some folds of cloth as a compress, the cavity was obliterated within a week, so that there was only a slight collection immediately around the opening made by the knife. Attention was next directed to the abscess of the thigh, which was treated in the same manner as detailed in the case of the lumbar abscess; but, owing to the permeation of the fascia and intermuscular spaces by the purulent collection, the result was not so favorable. There was still considerable induration of the deep structures, as was perceived upon palpation; and the original opening had not closed. As proper compression around the entire limb could not be made without impeding the circulation, it was not practicable to effect such approximation of the walls of the pyogenic membrane as to agglutinate them. Upon the dorsal surface were observed the indications of the openings of other abscesses, but of much less extent than the two which have been mentioned; and there were no new developments of a purulent nature. As this condition is attributable to the altered state of the secretory and absorbent apparatus along with impaired nutrition, the aim throughout was to restore tone to the organization and correct the deteriorated condition of the blood elements. The patient was given Lugol's solution of iodine and iodide of potassium continuously, with extract of malt during the first month. This was followed by the syrup of iodide of iron and cod-liver oil, with the most nutritious food; but as an œdematous condition of the extremities with puffing of all parts of the body ensued, one-fourth grain of the protiodide of mercury was ordered three times a day, and, with the continuation of this for ten days there was no longer any œdema, while the general appearance materially improved.

The immediate or exciting cause of the multiple abscesses in this case was doubtless embolism, since they were not the result of any local irritant, nor could they be attributed to micrococci. In the pus from cold abscesses, Rosenthal was unable to find any microorganisms; and, although there is much in favor of the idea that suppuration is dependent upon the presence of microorganisms, yet it cannot at the present time be stated as absolutely proven. In the adynamic state of the vasomotor system of nerves connected with the atony of the circulatory apparatus, both central and peripheral, attending the general prostration under which this man labored for more than a year, it is a fair inference that some thrombosed vessels

existed, which originated this trouble, accompanied with scrofulous cachexy. We had now relieved the local effects by the evacuation of five different collections of pus, but the more difficult task of correcting the widespread deterioration in the nutritive functions was yet to be accomplished. The disorder was not local but constitutional, and had to be treated accordingly by remedies to recuperate the vital forces.

Lymphangitis originates frequently from slight abrasions or pricks independent of septic influences, but may occur with any unhealthy wound. Stephen Smith describes it as follows: "Lymphangitis may occur in any wound, and is due to a poison passing through the lymphatic vessels; this poison may be decomposed secretions from the wound, or putrid matters; it appears as fine red striæ, running longitudinally from the wound toward the swollen and sensitive glands; the limb is painful on motion; there are fever, loss of appetite, and general depression; the inflammation may terminate in resolution or in the formation of abscess at some point."

The details of a case formerly under our care will illustrate satisfactorily most of the phases of this malady.

Mr. A. J. S——, 40 years old, of robust constitution and enjoying heretofore good health, received on the 17th of March, 1887, a slight injury from a copper wire over the articulation of the first and second phalanges of the middle finger of the right hand, involving the superficial layer of the skin without any sanguineous discharge. It caused but little inconvenience at the time, but gave him some inconvenience that night, and on the following day the patient punctured a small festering point with his penknife, under the impression that a discharge would afford relief. The finger became painful and somewhat red, yet there was no swelling. He applied some camphorated spirit of turpentine without affording relief, and finding on the next day that the pain extended up the arm with an enlargement and soreness of the axillary glands, he sought medical advice.

March 19th, the patient presented a care-worn appearance with some febrile excitement and there was a red streak extending along the back of the hand and up the forearm with increased pain throughout the entire limb, yet there was but little swelling in the finger or hand on that occasion, while the glands in the axilla were considerably indurated and enlarged. We prescribed for internal use a compound of fluid extract of jaborandi one ounce, salicylate of sodium two drachms, and syrup of orange peel two ounces, to be taken in teaspoonful doses every hour; and for external application, belladonna ointment, smeared over the finger, along the arm, and upon the enlarged axillary glands every two or three hours. On March 20th, there was marked aggravation of the local trouble; the thermometer indicated 102° and the pulse was 110 to the minute, while the hand was swollen and the redness along the forearm was then defined. We prescribed sulphate of quinine, gr. xx., Dover's pow-

der and calomel each gr. xii. in four capsules, one to be taken every two hours; and belladonna ointment ʒi., with camphor ʒi., to be applied locally with poultices of flaxseed and hops to the hand.

On the 21st, there was a reduction of temperature to 100° and of the pulse to 100, but the finger was swollen and very painful, with seropurulent collections beneath the outer layer of the skin on its dorsal aspect, which were discharged by punctures. Ordered to resume jaborandi and salicylate of sodium. In the afternoon the inflammatory indications had become more aggravated and the fever continued, without any free evacuation from the bowels for twenty-four hours. We ordered the following mixture: Infusion of serpentaria ten ounces, syrup of rhubarb two ounces, tincture of aconite twenty drops, and sulphate of sodium one ounce, to be taken in doses of a wineglassful every hour until the bowels were moved, and afterwards at longer intervals. A liniment of spirit of turpentine, six ounces, and camphor, three drachms, was applied to the entire arm.

On the 22d, all the symptoms were of a more serious order, but the cathartic had had the desired effect. We then gave sulphate of quinine, gr. xx., with camphorated Dover's powder, gr. xii., in four capsules, one every two hours. For local treatment, we ordered flaxseed and hops to the hand with the addition of Peruvian bark and charcoal to the poultice enveloping the engorged finger. The camphorated turpentine liniment was continued to the hand, arm, and axillary glands.

On March 23d, the temperature was normal and the pulse 70 to the minute, but there was a tendency to general prostration, and there were indications of loss of vitality in the finger. A tonic and recuperative course was adopted with the use of fluid extract of malt day and night, and a mixture of a decoction of Peruvian bark twelve ounces, tincture of nux vomica half a drachm, and chlorate of potassium two drachms, half a wineglassful to be given every two hours. The constrictions at the joints of the finger being considerable, with diminution of the natural heat at the extremity, free incisions were made on the palmar aspect of each articulation, and also on the dorsal aspect of the metacarpo-phalangeal junction; these permitted the escape of ill-conditioned pus from the last-named opening and from that in front of the same articulation. The Peruvian bark and charcoal with flaxseed and hop poultices, kept hot by frequently renewing the application, were diligently employed on the finger and hand, while spirit of turpentine with camphor was poured into the incisions at each dressing.

On the 24th, it was evident that the first phalanx of the middle finger had lost its vitality, and the patient was informed that an operation would be requisite, but that it was preferable to wait for the line of demarcation to be established before amputating the finger. On the 26th, the line of separation being defined between the gangrenous and living tissue midway of the second phalanx, the finger was amputated by disarticulation from the metacarpal bone.

Upon the withdrawal of the pressure from the brachial artery it was observed that no jet of blood occurred in the wound, but that there was copious oozing from several points. As the application of

hot water did not control this bleeding, we saturated a compress of absorbent cotton with camphorated spirit of turpentine and arrested the oozing. The patient made an uneventful recovery.

In another similar case, resulting from a slight wound on the dorsal aspect of the first joint of the middle finger from the front tooth of an individual who was struck in the mouth, gangrene of the first and second phalanges occurred, and the lymphangitis extended to the armpit, with great constitutional disturbance. The finger was amputated at the metacarpal joint and the case terminated well.

While living in Brazil the writer was once called to treat a woman who had slapped her daughter in the mouth by a backward blow; the fourth finger was slightly injured by a tooth, and a lymphangitis occurred, terminating in ankylosis of the joints of the finger.

The symptoms of pyæmia are well described by Braidwood, from whom we quote the following summary, which gives us a clear account of the ordinary course of the disease: "Commencing suddenly, generally with rigors and pyrexia, sometimes with a depressed and anxious countenance, we next observe the patient suffering from bronchitis or pneumonia, profuse perspirations, a dusky and icteric discoloration of the conjunctivæ and skin, a peculiar heavy or purulent (before called sweet or hay-like) odor of the breath, disinclination to food, extreme prostration, restlessness, then muttering, and lastly maniacal delirium, a rapid pulse, and increased temperature of the skin. These are the constitutional symptoms which characterize this disease, and which are accompanied by the formation of secondary abscesses in the joints or beneath the skin; while the wound (if present) becomes stagnant, its granulations look glazed, the discharges become sanious, offensive, or of a bluish-green color, and the edges gape. Except in the acute form, where the fever becomes aggravated or diminished in severity generally on the seventh or eighth, on the fifteenth, the twenty-first, or twenty-second, or on the twenty-eighth day after its commencement, one of the peculiarities of suppurative fever is the absence of nearly all respect to time which it exhibits."

With regard to the existence of critical days, as pointed out in this description, to establish the existence of which Braidwood adds a long table in his appendix, Ashhurst says that his own observation would tend to show that there are none such in the course of pyæmia, nor do this author's statistics bring the same conviction to Ashhurst's mind that they apparently bring to his own.

It should also be added that acute pyæmia not very seldom runs its course to a fatal termination in four or five days, or even less. In addition to the symptoms above enumerated, vomiting is occasionally a distressing accompaniment of pyæmia. Diarrhœa or

dysentery, or occasionally constipation is present. The urine is generally albuminous, and sometimes contains pus. In the matter expectorated, Braidwood has found broken-down lung tissue. Various cutaneous eruptions are occasionally observed, which he attributes to the existence of capillary thrombosis. Acute pain and hyperæsthesia precede and attend the development of the secondary joint affections, and have always seemed to Ashhurst to present a strange analogy to the same phenomena as observed in cases of arterial embolism or deligation.

The progress of *suppurative fever* presents no points which call for especial comment. Braidwood describes four stages of the affection, viz., that of incubation, that of invasion, the typhoid stage, and the stage of convalescence.

Varieties.

Septicæmia is a constitutional, generally acute disease, popularly called blood poisoning; due to the absorption of various putrid substances into the blood, which are supposed to act as ferments and so to change it that it cannot fulfil its physiological functions. The lymphatic infection is a form of septicæmia in which the infecting material has entered the circulation by way of the lymphatics; it is rapid and severe in its course and characterized by effusions into the several cavities. Peritoneal septicæmia is a form that may occur and prove rapidly fatal in consequence of a wound of the peritoneum with or without peritonitis. Puerperal septicæmia is due to septic infection in the puerperal state. Venous septicæmia is that in which infection proceeds from a putrid thrombus as in uterine phlebitis.

The most serious form of septicæmia which is encountered in surgery is that in which the toxic influences extend to the nerve centres with but little local manifestation in the tissues involved, excepting the loss of vitality. This overpowering impression prevents the ordinary inflammatory developments in the adjacent structures, and instead of there being hyperæmia of the area involved, a necrosed condition is observed, which is speedily followed by general collapse with subnormal temperature. This insidious progress of the toxæmia may escape attention at the outset and become notable only when the gravity of the symptoms indicates an early fatal termination.

It may be inferred in these cases that such a transformation is produced by the development of ptomaïns in the part affected that mortification ensues; and although the patient does not suffer pain, this lethal impression is propagated through the nerve centres to the vital organism. While stimulants of the most energetic character are

indicated under such circumstances, they are found insufficient to avert the death of the patient.

In that class of septic manifestations known as *dissection wound* the absorption of the decomposed elements from a dead body presents in a typical form the action attributed to ptomaïns. There is a concentration of malignant death-dealing energy; and its destructive force is exhibited by the smallest appreciable particle of the ptomaïn which may enter into the organism. The ptomaïn possesses a most extraordinary toxic property, which diffuses itself through the lymphatics and results in the disorganization of remote as well as neighboring structures. The most serious consequences ensue from the slightest abrasion of the cuticle, which admits of absorption of the toxic element, and it is rare that its progressive work of destruction can be arrested without disintegration of the tissues involved. Those who witnessed the influence of dissection wounds before the introduction of the practice of antiseptic injection of dead bodies need not to be reminded of the grave results, and those who have incidentally met with instances in recent times must be profoundly impressed with its terrible agency for disorganization of vital structures.

We are informed that *pyæmia* usually follows wounds, suppurative inflammation of bone, or childbirth, and results in the formation of secondary abscesses in the viscera, joints, and connective tissue, and that it is sometimes associated with phlebitis or embolism. But this term is applicable only to those cases in which pus enters into the circulation. The morbid effects from other sources may be designated as *toxæmia*, being the result of some toxic agent of a different kind, but should not be included in the category of pyæmia. Thus it turns out that the cases of blood poisoning may be numerous in which the element of purulent infection does not exist. It is true that cases of pyæmia without any discoverable lesion have been reported, and it is hence inferred that the condition may occur as an idiopathic disorder. But in this as in tetanus, the weight of evidence is in favor of a local origin, and it is in many instances difficult to detect the focus of suppuration. The development of pyæmia cannot take place without the previous formation of pus, which becomes absorbed by the lymphatics.

The studies of Virchow concerning thrombosis and embolism showed that the changes in the veins which had been regarded as due to phlebitis were caused by the coagulation of the blood, and by subsequent degenerative changes in the thrombi thus formed; that the infarction and the abscesses seen in the veins were due to emboli which had become detached from the softened thrombi, that as the

white blood globules and pus globules were identical in appearance they could not be distinguished, and that it was improbable that pus globules should find their way into the blood.

On the other hand, Sedillot, Weber, Billroth, and others have held that laudable fresh pus was capable of being absorbed and of producing a febrile movement. Panum has been quoted in support of the view that the poison might be one of the chemical products of putrefaction; his investigations led to the conclusion that there is in putrefying fluids a specific chemical substance, soluble in water. This substance, if introduced into the blood, produces the peculiar symptoms which belong to what is usually called putrid or septic infection, and it possesses these properties even after being freed from all microscopic organisms.

It is no longer held that pus enters bodily into the circulation except in the event of ulceration of the venous walls; but the contact of pus with the lymphatics leads by a pathological process to septic absorption, and hence to general contamination of the system. The experiments which have been resorted to for distinguishing between the white corpuscles of the blood and pus corpuscles have not afforded definite results, nor has the hypothesis of a third blood corpuscle availed anything towards a solution of the problem connected with purulent infection.

The fact of a toxic influence being conveyed by pus through the lymphatics to the vascular system is recognized generally by pathologists, and while the link which connects cause and effect has not been clearly established, the clinical relation is sufficiently definite for all practical purposes. The collection of pus in the internal organs when confined by a pyogenic membrane may develop hectic fever, which disappears after the evacuation of the abscess, but the removal of a purulent focus of absorption does not always arrest pyæmia.

Sapræmia is the name recently given to an infection resulting in symptoms of less intensity. The saprophytes associated with this condition are such as will not exist in blood or living tissue, but flourish in necrosed tissue and decomposed blood clot or pus. The time usually required for the symptoms of sapræmia to be manifested is from two to three days after infection. The disease is therefore slowly developed when compared to pyæmia and septicæmia. It is more localized than pyæmia, and rarely develops into multiple abscesses if the infected matter is removed. Senn, Park, and Wharton all make use of the term sapræmia, but with their individual coloring as to its meaning. The idea of a distinction of living and dead tissue seems to prevail with Senn as distinguishing it from septicæmia.

The initial chill which often exists in septicæmia is reduced to chilly sensations when the case is one of sapræmia. Pyrexia may exist but is soon reduced by the institution of drainage. Instead of a high temperature and a rapid pulse, we have a flushed face and an indisposition to work. The bowels may be constipated and later they may be loose.

The condition known as typhoid describes the impairment of the nervous, vascular, and lymphatic systems. In many cases erysipelas, diphtheria, carbuncle, and scarlet fever also so poison the system as to leave a state of sapræmia. The most usual cause of sapræmia is retained placental tissue—an absorbing surface favoring intoxication. A cavity which may have little or no exit favors the decomposition and the rapid local contamination of the absorbing surface, and usually predisposes the patient to infection.

Diagnosis.

The diagnosis between septicæmia and phlebitis may generally be made by noting the involvement of the ganglions in lymphangitis, which is not always confined to the first ganglion in the tract of the absorbent vessel. It may be observed that the initial lesion which leads to the development of lymphangitis is not generally characterized by any marked signs of local inflammation or accompanied by the formation of pus at the seat of injury.

Immunity and Susceptibility.

Immunity to the constitutional results of traumatism may be conferred by previous inflammatory processes, and increased susceptibility to certain forms of inflammatory action may occur from slight superficial injuries. The development of lymphangitis from a slight abrasion, involving the minute ramifications of the nerves and capillaries, has been attributed to the ganglionic element which is supplied to the rudimentary structure of the connective tissue.

The peculiar consequences of punctured wounds and small lacerations of the integument, developed in the form of tetanus, are dependent upon the action of ptomaïns, and it is very rare to find open, frankly suppurating wounds followed by tetanus.

There must exist not simply a susceptibility on the part of the general system, but a very marked predisposition to take on an impression from local injury, in cases in which lymphangitis or tetanus is developed in such lesions.

Under different conditions, it is found that pyæmia and septicæmia

follow traumatism. A distinction should be recognized between the normal and physiological condition of the nerves and blood-vessels in recent injuries, as compared with the abnormal and pathological state, resulting from inflammation or other structural disorders of any portion of the organism.

To appreciate the changes wrought in the tissues by inflammatory processes, it becomes necessary to look into the composition of the different textures of the organism.

The cellular constituents of muscles, blood-vessels, nerves, and serous and mucous membranes undergo modifications through inflammation, which render these structures less disposed to resent the impression made by a surgical operation than is observed in normal tissues. How far the presence of microbes and the process of phagocytosis may operate in modifying the condition of the tissues, under the course of inflammation, must be considered in any serious study of immunization.

The sphere of antisepsis, as now recognized, is to correct a tendency to or a development of degeneration and disintegration of living structures, resulting from contamination in any form. If we are able to discover the causative element and neutralize it by antiseptic measures of a topical or a constitutional nature, this is eminently proper. But in default of identification of the cause, it devolves upon us to combat the injurious effects of the vicious impression already made upon the organism, and this is the special province of antiseptic surgery, instead of seeking to anticipate trouble by the use of germicides.

The measures formerly regarded as belonging to antiseptic surgery included many supposed to be preventive which proved to be disturbing influences, so that instead of protecting the organization, by immunization, they produced derangement of the system and led to septic developments. Having the courage of his convictions based upon investigations of this subject, the senior author has always protested against a blind acquiescence in what has been erroneously styled antiseptic surgery, and it gives him great satisfaction to know that his position is sustained by the best men in the profession at the present time.

The cases of poisoning resulting from even the most cautious use of carbolic and bichloride solutions call for their abandonment in surgery. It is this class of agents which we have placed under the division of septic surgery, instead of antiseptic surgery.

The point is settled beyond controversy that these are potent germicides, but in the race after microorganisms more damage is done to the structures in which they are supposed to be located than

the microbe is capable of doing if let alone. The great dangers resulting from the contact of solutions of carbolic acid and corrosive sublimate with recently cut surfaces are now so well known to the profession throughout the world that it is unnecessary to specify instances to any reader of current literature. We feel, therefore, that surgeons who continue to employ solutions of these poisonous drugs are without a shadow of excuse, and should realize that they are not practising true antiseptic surgery, but septic surgery. The consideration should come home to them that asepsis has taken precedence in surgery involving normal structures.

At a recent meeting of railway surgeons some views were expressed indicating that there is something calling for antiseptic surgery in the treatment of railway accidents which does not exist in the case of other injuries. Why lacerated and contused wounds received in a collision or in any other manner connected with a railway should differ from a similar injury inflicted under other conditions is quite incomprehensible. The great point made that the difficulties in the way of practising asepsis render it important to adopt antiseptic measures, preliminary to carrying out aseptic treatment, does not avail against the claim of bacteriologists of good standing, demonstrating that the use of germicides in uncontaminated structures proves generally injurious to the tissues.

As regards the injuries from accidents in riding bicycles, it has been asserted that in this class of wounds, as in those connected with railway surgery, there are some special features by which they are to be contradistinguished from other lesions of the tissues. A writer in *The British Medical Journal* states that the "cycle graze is very troublesome to heal. The two upper layers of the skin over some bony prominence are killed by the blow from the fall, and the resulting sore, if neglected, often remains open for weeks." Other comments are made upon the distinctive character of the wound, but the author admits that the injuries sustained from cycle accidents do not differ in any essential particular from those caused by other falls from swiftly moving carriages.

It is prudent policy to rely upon the *vis medicatrix naturæ* to a large extent in the management of violent traumatic accidents, and there is a masterly inactivity which avails much towards the restoration of structures that have been seriously injured without material impairment of vitality.

The province of asepsis in such cases is proper adjustment of the structures and the prevention of everything likely to interrupt the curative process. It is doubtful if anything is better than the blood plaster from the saturation of a roller around a fresh cut on either the

hand or foot. The parts are in their normal state, with a good prospect of healing if let alone, and meddlesome surgery can only interfere with the curative process, so that "hands off" is the true policy in this class of cases. With his present lights and with the resources at his command, the surgeon is warranted in undertaking to save limbs which under the old régime were necessarily sacrificed. But we should not try to save a dead member, it being our duty to lop off what cannot be restored to life.

Asepsis is the prevention of all contamination from within or without in the treatment of wounds, and the most extensive traumatism may yield a good result with the proper use of aseptic measures. Among aseptic resources the most important then is cleanliness, which John Wesley declares to be next to godliness. The idea conveyed by freedom from dirt or filth applies not alone to the absence of any foul or extraneous matters from the wound, but to its complete removal from the surroundings of the apartment. Of course, the clothing and bedding of the patient should be free from blot or stain or any such thing.

Yet, withal, it has been questioned whether those who have been accustomed to live in the midst of filth can be entirely removed from such surroundings without a protest of nature against such a revolutionary measure. It is even held by some gynecologists that women whose houses are not models of hygienic requirements bear up under a laparotomy at their own quarters better than in the best regulated hospital. Our personal experience in undertaking the management of cases requiring extensive incisions for the removal of large ovarian tumors in private quarters has been entirely satisfactory, and we doubt the advantages claimed by some operators for hospital surroundings in laparotomy. One of the gynecological staff at the Grady Hospital, Atlanta, remarked on one occasion that his results in abdominal surgery in women had been more favorable in cases operated upon at the patients' homes, however humble, than in the hospital. We have not at hand the statistics of the gynecological work in the Grady Hospital, but the general impression of the profession in Atlanta is that there is a much larger mortality in laparotomies done there than in the same kind of operations in private practice. The most feasible explanation of the lesser mortality in private practice is the comparative immunity conferred by observing, more or less, the habits of life to which the patient has become accustomed.

We witnessed a striking illustration of the effect of habit, a few years since, in a lady sixty years of age, upon whom we operated for the removal of an immense cystic tumor of the ovary. Everything progressed well for a day or two after the operation, when the

patient's listless and depressed condition attracted the attention of all around her, and upon inquiry it was ascertained that of her own accord she had given up her habit of using snuff since the operation. The patient was directed at once to resume the use of snuff, and within twenty-four hours she had undergone a most favorable change, and continued to improve without any further drawback until completely restored to health.

There is no doubt, also, in regard to the use of spirituous liquors habitually by those who undergo surgical operations, that a sudden interruption of this indulgence exposes the patient to disturbances of various kinds. Those who have been excessive drinkers of ardent spirits have their vitality so much impaired by its effect upon the organism that they do not resist the shock to the general system from operation so well as others who have led lives of abstinence. But the immunity of habit avails for those who have indulged moderately in the use of intoxicants and a modified use after surgical operations is indicated. This, however, gives no security corresponding to the immunization of a vigorous normal state of the organization, such as is found in perfect health, when there is a proper performance of all the functions of the body.

The law of habit comes into play still more distinctly in those who are victims to the use of opium to an extent that their nerve centres are very materially affected by it. In all such it may be laid down as a rule for the guidance of the surgeon that the habit must be respected, by its continuance for a time after operations are performed.

Yet the possibility of overcoming a habit after the immediate cause for its use has been removed by operation was exemplified in a recent case. Mrs. A. E. C., aged thirty-six, had experienced great pain from the recurrence of a carcinoma of the antrum. She had been in the habit of using one grain of morphine daily. This was kept up before the operation, but she was able to stop the use of it a few days after the operation.

The study of serpent poisons is particularly suitable for increasing the precision of our knowledge with regard to toxins, both on account of the direct analogy which the one presents to the other, and also because of the greater rapidity and precision of the action of serpent venom, which allow the physiologist to make infinite variations in his experiments without exposing him to sources of fallacy surrounding the investigation of toxins arising from different cultures, or the employment of animals whose individual resistance in respect of certain poisons is very variable. Experiments published since 1893 by Calmette have established:

1. That poisons of venomous animals in different parts of the world present very direct analogies with each other, and that an animal artificially immunized against a very active poison (*e.g.*, that of the cobra) is also refractory to all less active poisons.

2. That the serum of animals protected against large doses of very active poisons possesses protective and curative properties so intense that it is capable of conferring in a few minutes on fresh animals absolute insusceptibility to all these poisons.

3. That the amount of curative serum that an animal (such as the guinea-pig, the rabbit, and the dog) should receive, when inoculated with a venom, is inversely proportional to its weight, and directly proportional to the amount of venom received.

Calmette has conducted at the Pasteur Institute of Lille a series of experiments to determine the part played respectively by the nervous system, the leucocytes, and the various fluids of the organisms in the production of artificial immunity against venoms. He reviewed the researches of Fraser regarding the preventive potency of bile, glycocholate of sodium, cholesterin, and the tyrosin of the carrot or dahlia tubers against serpent venom, comparing the effects of those substances with those of antitetanic serum, the serum of dogs inoculated against hydrophobia, certain normal serums of the horse and dog, and even in some cases normal beef bouillon freshly prepared. An investigation was made to determine whether in these cases a true immunity of greater or less duration was afforded, or simply a cellular resistance more or less transitory and devoid of any specific character.

In respect of bile, Calmette found that this secretion undoubtedly possessed, as asserted by Fraser, the property of destroying the venom in vitro. All the venoms, as well as certain microbic toxins, that of tetanus for instance, when left in contact for forty-eight hours with a certain quantity of fresh bile, lost their toxicity. Heating the bile to a point short of 248° F. enfeebled but did not destroy its toxicity. But when the bile was injected forty-eight hours before the venom, even in doses relatively large (*e.g.*, 1.5 to 2 c.c. of ox bile for a guinea-pig weighing 500 gm.) no preventive action was observable, neither was any therapeutic effect noticeable when it was injected after the venom, thus clearly showing that it was the admixture only of these substances which was effective in destroying toxicity.

Particular attention was called to the necessity for employing on the check animal doses certainly fatal in two or three hours; for when doses fatal only in five or six hours were employed, about four out of ten guinea-pigs were found to recover from the illness produced without the aid of any preventive injection. Injection of the venom into the gall-bladder of rabbits caused death after a protracted inter-

val, probably because the venom was absorbed before the bile had had time to act.

Cholesterin dissolved in ether was found to possess no real protective power, though it retarded death for from one to five days when injected from two to four hours before a dose of venom ordinarily fatal in three or four hours. If injected forty-eight hours previously, it was without effect.

Similar effects to these, it was found, were produceable by different substances (*e.g.*, fresh normal bouillon, certain serums, normal, antitetanic, or antirabic, etc.). But this could not be regarded as indicating any real specificity; it should rather be regarded as transitory stimulation of the leucocytes whose mission was to seize and hold the venom. The important rôle of the leucocytes was shown by the facts that the injection of venom was always followed by an increase of leucocytosis, and that a dose of venom slightly diluted with fresh leucocytic exudation invariably retarded the intoxication.

In regard to the nervous system, emulsions of neither rabbits' nor serpents' brains exercised the least antitoxic power either in vitro or in the living animal. Experiments were also made to see if the injection of certain substances (*e.g.*, curare, chloral, strychnine sulphate, etc.) known to act energetically upon the cerebrum, the cerebellum, and the spinal cord, would destroy the passive immunity of rabbits produced by antivenomous serum, and it was found that they did not. Calmette concludes as follows:

1. The action of bile, cholesterin, etc., as well as that of certain, not all, antitetanic, antirabic, and other serums, cannot be regarded as a true antitoxic action in regard to venom. It is simply a means of cellular stimulation whose effects are very transitory, and which can be produced by very different substances.

2. After the injection of antivenomous serum, the serum manifests its protective action, notwithstanding that the resistance of the nervous elements may have been diminished by the injection of various poisons which act upon them.

Prophylaxis.

The complete drainage of pyæmic abscesses is important for the reason that reabsorption of the pus is very liable to occur. The pyogenic membranes are not absorbing surfaces as a rule, but the scraping and medication will not avail when the cavity has a small opening and is kept for days plugged with iodoform gauze in the vain hope of the capillary drainage secured. Frequent dressings are necessary and through and through drainage, in all cases of closed

cavities, such as we have in putrid empyema and in pelvic abscesses.

Many reports have been made recently to medical societies and published in journals of cases treated by the antistreptococcus serum, some successfully, others unsuccessfully. The cases treated by this process should be carefully studied and the results recorded should state specifically what was the character of the pus found and what particular culture of immunizing serum had been used. The question of prophylaxis is certainly much more important than that of treatment, in the present state of our knowledge. The injection of antitoxin serum for diphtheria is on a much more scientific basis than that of antistreptococcus serum for pyæmia, inasmuch as the Klebs-Löffler bacillus was certainly isolated and the etiology proved several years before the antitoxin treatment was undertaken.

The supposition that immunity results from local applications to the field of operation has led to the use of antiseptic dressings with a view to prevent contamination. But further observation has convinced operators that no favorable influence is exerted by germicidal washes upon normal structures, and that the only indication for antiseptic applications is to combat existing septic conditions.

A very interesting illustration of the effect of antiseptic substances is given by Henggeler in a report of 276 cases of strangulated hernia operated upon at Zurich from 1881 to 1894. During the period of the use of carbolic acid as an antiseptic (*i.e.*, from 1881 to 1885), 38.15 per cent. of the patients died; during that of bichloride (*i.e.*, from 1885 to 1893), 21.1 per cent. died; and since the introduction of aseptic methods only 16.3 per cent. have died. In 48.4 per cent. of the 64 fatal cases, the cause of death was gangrene of the intestines and peritonitis, but there is nothing said as to the influence of antiseptics in producing these troubles.

It is the accepted doctrine now that asepsis secures greater immunity from contamination than antisepsis in surgical operations upon structures in their healthy physiological state, and few operators follow the practice of five years ago by resorting to germicidal applications to fresh cut surfaces.

The senior author occupies the same position which has been held by him during all the vicissitudes of the war against germs, and the most advanced views of bacteriologists are now exactly in unison with the doctrine he has advocated from the outset of this controversy. His course has not been a tacit acquiescence in what was maintained by others, in regard to the hurtfulness or otherwise of all germicidal applications upon fresh cut surfaces, but at all times and in opposition to the tenets of colleagues with whom his lot was cast, he has openly

spoken out his convictions as to the injurious effects of carbolic acid and bichloride of mercury solutions in connection with operations on normal structures, and he has consistently maintained that their use was admissible only in septic conditions.

A normal, healthy structure does not call for the application of germicides, but when the tissues have undergone contamination antiseptic applications are requisite. It is held by some strenuous opponents of poisonous drugs that innocuous agents may be employed as antiseptics with a satisfactory result. Yet it is the practice still with some members of the profession to employ solutions of carbolic acid and corrosive sublimate upon delicate tissues without regard to the serious results of their absorption.

There is a phase of septic development to which potent germicides are applicable, and when a local source of contamination exists, whether it is associated with bacteria, fungi, or ptomaïns, the most vigorous use of antiseptic measures is demanded. It is evident that septic processes, which uncontrolled would lead to septicæmia, are arrested in many instances by correctives of various kinds, and a prompt resort to antiseptics and germicides is indicated to arrest the progressive contamination of the general organization from the local septic process.

Arloing and Chantre hold that the essential agents of purulent surgical infection are the ordinary microbes of suppuration. Should other microbes be present in the lesion with any frequency they are to be regarded in the light of complications, and not as necessary factors in the development of the purulent infection. A purulent infection can result only when the streptococcus (the authors confine themselves to that form) is endowed with the same virulence as it possesses in the acute and severe forms of puerperal septicæmia, and not with that which it exhibits in single phlegmon or erysipelas.

Though etiological relations between purulent infection, puerperal septicæmia, and erysipelas may be suspected, yet it cannot be proved where and how the change in the pathogenic properties in the streptococcus, productive of different clinical conditions, is effected.

E. L. Keyes says that healthy urine is sterile, while purulent urine is always microbic, and that microbic infection takes place from within the body by a number of methods in the course of disease; it is often brought about by the instrumental maneuvres on the part of the surgeon. A healthy organism, the bladder being vigorous, may cope successfully with such microbic invasion, and rid itself spontaneously, or with a little aid, of all damage arising therefrom, showing little or no inflammatory response. A suitable condition of the patient's soil is essential to the propagation and perpetuation of inflammatory phe-

nomena upon the urinary tract—after microbic invasion. This condition, intensified by traumatism and physical weakness, notably of degenerative variety, is most intense where there is vesical distention with atony, and when the ureters are dilated and the kidneys involved in the changes incident to tension below—namely, atrophy and sclerosis above, with or without surface catarrh.

Under these circumstances surgical pyelonephritis is most likely to declare itself as a result of microbic infection from below (occasionally from above) in the course of suppurative disease or after operative interference. Asepsis, antisepsis, and sterilization of urine are ends to be aimed at in genito-urinary surgery, but, like all other greatest goods, are not yet attained in perfection.

That micrococci are associated with the progress of diseases involving the different structures has been demonstrated clearly by the microscope; and experiments tend to prove that certain disorders are propagated from one person to another by means of such germs. The modes adopted for testing the introduction of microbes into the system have not afforded any conclusive evidence as to the etiological factor in the development of morbid products. But the observation of bacteriologists has gone very far towards establishing the existence of special forms of bacilli in different types of disease. Whether these various modifications of the bacterial order enter as a causative element, or simply as a concomitant of the several disorders with which they are associated, has not been satisfactorily elucidated.

If the investigations should be conclusive in regard to the constant appearance of distinct bacilli in a large proportion of diseases, so as to serve the purpose of diagnosis, it would conduce greatly towards placing medicine and surgery upon a scientific basis. This being attained, the next step to be aimed at is the therapeutic measure which may prove efficacious in eliminating these morbific agents from the different structures of the body and correcting their ravages in the organs.

A grave point for consideration in connection with the development of bacteria in the physical organization is whether they are hurtful in the living condition or after losing their vitality and acting as ptomaïns in the organs. If the analogy of the growth and the decay of hydatids in the tissues can hold in the case of bacteria, it may be inferred that the chief harm results from their death and decomposition.

A very interesting view of the relation of leucocytes to bacteria has been presented by Sutton, who claims that an interminable war is carried on between these infinitesimal antagonists in the organization. If the former prevail health is secured, but in case the latter

exert a controlling influence, the result is disease. The object of medical science is to aid the leucocytes.

At this time the medical profession is undergoing a most interesting transition from the extreme views which have been held by some in regard to the employment of germicides in surgical practice. There was a time within the past decade when it was deemed to be scientific and progressive to use antiseptic measures of the most energetic kind in all operations, whether there was a septic element to combat or not. But thanks to the mature investigation of the effects of germicides upon normal structures by bacteriologists of the highest order of qualifications for this class of work, it has been demonstrated that the so-called antiseptic agents are capable of setting up septic processes in healthy tissues. The tables are now turned, and instead of a surgeon being compromised by eliminating germicides from his surgical procedures in ordinary cases, and confining his irrigation of recent wounds to simple sterilized water, it is the one who departs from this course by the employment of solutions impregnated with toxic agents who is held responsible for the consequences of the absorption of these poisons. There was a time, and that recently, when prominent members of the profession would have gone into a court of justice and testified that another physician or surgeon who had failed to use the so-called antiseptic treatment in a given case had failed to do his duty, even if he was not liable to a charge of malpractice.

But let us consider where this conservative practitioner now stands with the development of science in the researches of bacteriology. When there is a septic contamination in a part, germicides are indicated for the correction of this vitiated condition and should be carried no further than requisite for this purpose. But in case there is a healthy and normal state of structures involved in a cutting operation, there can be no indication for antiseptics and their use is only calculated to do harm by absorption, and the best men in the profession have ceased to employ them.

The most energetic, and hence the most likely to cause mischief, is corrosive sublimate. In a paper by Dr. Ap Morgan Vance, of Louisville, in the *Medical and Surgical Reporter*, it is stated that three years ago Welch, of the Johns Hopkins University, made a report in which he mentioned numerous experiments with sublimate made with a view to find out something about the action and power of this drug. "I think," says Vance, "it is proven beyond all doubt by his experiments and by those of his attendants, particularly Abbott, that the present position of bichloride is rather against its use, and that it does more harm than good. If the solution be of sufficient strength to have

any effect upon germs already there it will cause necrosis and prevent healing of the wound as well as produce a better nidus for the production and operation of the microorganisms." In the light of these and of other experiments mentioned in this paper, it is plain that for use in surgical practice the solutions of corrosive sublimate do not possess the advantages hitherto attributed to them. We may be allowed to refer those who still cling to this idol to the practical remarks of Dr. Vance on this subject, as follows: "Two years ago I ceased the use of solutions, particularly in fresh wounds, and have lately ceased to use them at all, even in suppurating conditions. I have found in my practical work that since I ceased the use of sublimate solutions I have had much more uniformly good results by using simply sterilized water."

In his address at the opening of the session of the Southern Medical College in 1888 the senior writer made his position clear upon this subject in the following words: "With the lights before the profession in regard to the cases of poisoning resulting from even the most cautious employment of recognized dilutions of both carbolic acid and bichloride of mercury in surgical dressings I am forcibly impressed with the conviction that they should be discarded in all operations upon normal structures." In the discussion upon aseptic and antiseptic surgery before the Medical Association of Georgia in 1890 he used this language: "The excessive use of carbolic acid and corrosive sublimate as washes to absorbent surfaces cannot be otherwise than hurtful; and the practical results in setting up disorders of various kinds, with not a few fatal results, should be a warning to surgeons against the unnecessary employment of these agents."

The prestige of antiseptic surgery was such ten years ago that a surgeon who dared to neglect the recourse to germicidal applications in his operations was styled an old fogy and unworthy of recognition by those of the advanced antiseptic practice. The zeal in propagating what was called Listerism reached such a point that a surgeon who might have an untoward result without observing its tenets would have had the testimony of its defenders against him in a suit for malpractice, and he would have been placed in a most embarrassing attitude before the medical world. But a change has come over the spirit of the surgeon's dream at the present day, and instead of being on the defensive, the opponent of germicidal washes in normal structures is now occupying the offensive position. The leading bacteriologists to-day are supporting him in condemning all poisonous applications, excepting only to wounds already contaminated which call for correction by antiseptics. In these alone is the so-called antiseptic surgery warranted.

The high authority of the Johns Hopkins faculty, headed by Welch, is arrayed against the employment of any germicidal or prophylactic solutions in operating upon normal structures, and sterilized water only is used in washing fresh cut surfaces. In a very instructive discussion upon the radical operation for hernia before the Southern Surgical and Gynecological Association at Louisville, Dr. Howard A. Kelly criticised the technique of a colleague, who thought it proper to conduct the entire operation under irrigation with a weak sublimate solution. "I would urge him," he said, "to abandon the use of solutions of the bichloride of mercury. The value of the inhibitory power of this drug over germ life is more than counterbalanced by its necrosing effect upon the tissues." Notwithstanding the most pronounced expressions of those best qualified to judge of the injurious effects of irrigation with mercuric solutions, it is found that some members of the medical profession continue to use them from force of habit, and they must learn by bitter experience to abandon the error of their ways.

The elementary and fundamental question in regard to the animal or vegetable nature of the germs of disease occupied bacteriologists for many long years; and though it has been finally accepted as the established doctrine that most of these germs are of vegetable origin, we cannot rely implicitly upon the results of this investigation. The division of microorganisms into the coccus, bacillus, and spirillum gives the starting-point for a multitude of subdivisions, and the vocabulary is constantly increasing as new workers come into the field. A recent writer thinks it may eventually become possible to neutralize the effect of the most deadly microbe by generating a variety inimical or destructive to it. By this achievement, bacteriology is claimed to have taken a new departure of which it is impossible to forecast the consequences in the future.

It is evident that many elaborate disquisitions on this subject are not based upon a personal knowledge of the facts, and the authors run into inconsistencies in explaining the outgrowth of their theories. The relations of bacteria to diseased processes in the organism depend to a very large extent upon the predisposition of the structures to take on disease, and upon the development of leucocytes which arrest the morbid element. It is held generally by bacteriologists that the predominance of phagocytes in the tissues which may be involved prevents the hurtful influences of bacteria and that the phagocytic process serves as a prophylactic against structural disorders. Indeed it is questionable whether active living microorganisms cause disease, and it may be fairly inferred that the loss of vitality in the micrococci is the source of trouble in most cases of morbid developments.

This lends force to the view that ptomaïns have an important rôle in the disorders of the physical organization, and the impression has been growing that this is the septic element in the suppurative and destructive results of any contamination from without. It is evident that ptomaïns contribute chiefly to the development of septicæmia in most cases. A ptomaïn is defined by Foster to be "an alkaloid formed as the result of putrefaction or abnormal fermentative changes taking place in an organ after death or as a consequence of morbid action during life. Ptomaïns are probably in all cases due to the decomposition of putrid or other organic compounds by bacterial action. Some ptomaïns are poisonous, others are physiologically inert."

An experiment has been made with peroxide of hydrogen and the ordinary preparation of permanganate of potassium, tending to show that both would act well in conjunction by the free liberation of oxygen. The peroxide of hydrogen should not be used in sinuses with no exit or in the abdominal cavity, as too much oxygen may be generated, and hemiplegia has resulted from pressure.

A thorough comprehension of the normal condition of the various structures which enter into the composition of the different organs of the body is a prerequisite to an understanding of their disorders and diseases, and some familiarity with biology and histology is, therefore, essential to one entering upon an investigation of septic troubles.

The practical bearings of pyæmia and septicæmia have cropped out in various forms connected with surgical work, and more especially in what has been designated as antiseptic surgery. This has been developed conspicuously by Lord Lister's method of treating surgical cases with special regard to the presence of septic features in the structures. His conception of the surroundings of a patient being attended with contaminations extending to the field of operation led to various antiseptic devices, and especially to securing cleanliness. Out of the vast array of elaborate dressings which were inculcated, little remains to-day of "Listerism" excepting the scrupulous avoidance of filth of every kind, constituting asepsis. In so far as the later experience of Lord Lister may guide surgeons in the use of germicidal agents for operations, all are aware that he now prefers carbolic acid washes to those of corrosive sublimate, and that they are employed with great caution. He confines the application of antiseptics to septic conditions of the parts involved and adheres mainly to cleanliness in the physiological state of the tissues.

Much credit is due to Lord Lister for drawing the attention of surgeons to the importance of avoiding contamination by filth of all kinds, but the large following he had formerly in antiseptic surgery has gradually decreased, until the vast majority of gynecologists and

surgeons of the present day rely exclusively upon aseptic measures in normal tissues.

Among those who have taken part in the study of bacteriology as allied to surgery, we have watched with great interest the development of the germ theory of the origin of diseases, and yet have not been so carried along with the current of opinion as to ignore entirely the fact that thus far it has not met all the requirements for comprehending pathological conditions. Without discrediting scientific experimentation, we hold that there is quite sufficient evidence that grave mistakes have been made in the mode of investigating the relations of cause and effect, connected with the presence of a microbial element in the different parts of the organism. That some diseases are uniformly accompanied with bacteria of a definite kind does not suffice to give a final decision as to the etiological factor in these diseases; and much less is it a conclusive indication for the therapeutic measures which are required for the relief of such disorder.

The general belief that experimentation upon inferior animals in their normal condition of health may be relied on as a guide in performing surgical operations upon the human being does not take into the account an important factor connected with the pathological condition of the structures. There may exist such modifications from acute inflammatory processes as to preclude an operation, or there may be present results of chronic inflammation of the tissues which shall prove advantageous by securing tolerance of surgical interference. The robust athletic subject, with strong proclivities to hyperæmia, while enjoying perfect health meets with an accident which interferes materially with the vital functions, and the local injuries call for operative interference at once. It is evident that a patient under such circumstances will not bear a surgical procedure so well as one who has become accustomed to the wear and tear of a slow inflammatory process which prepares the tissues for a resort to the knife.

Ashhurst states that "if the intermediate or inflammatory stage has come on, operative interference must, if possible, be postponed until the inflammation has measurably subsided, and until the patient's condition has become assimilated to that of a case of chronic disease rather than of traumatic lesion."

It is true, however, that secondary amputations give a somewhat greater fatality than primary amputations, being 45.5 per cent. of mortality in the latter, with 32.3 per cent. of mortality in the former, out of 2,755 cases tabulated from twenty-one different reports prior to the days of antiseptic surgery.

Hand disinfection by means of pure oil of turpentine is advocated by Boeckmann. He regards the chief protection afforded by turpen-

tine to be due to a species of varnish or filling in by it of the pores of the skin. His experience has been very satisfactory, especially when turpentine is used after thorough applications of soap and water, and of permanganate of potassium, or even bichloride of mercury. The chief thing in a surgeon's fingers is touch, and this tactile sense is destroyed and numbness is felt after the use of carbolic acid, but not after the stimulus of turpentine. Oil of turpentine is used to disinfect bedsteads, tables, floors, and all instruments used for operations. In an article on the "Medical and Surgical Uses of Spirits of Turpentine," the author has strongly advocated the use of this substance as a dressing for wounds and bruises of the skin, when the tissues are in danger of gangrene. The strong indorsement given it by us has led to a general use of turpentine by many physicians in the Southern United States, where it is cheap and readily obtainable.

The capillaries which are torn and mangled in contused wounds absorb the oil of turpentine, which acts as a styptic and restores the circulation by capillary anastomosis. The nerves in the pulpefied tissues of railroad accidents are stimulated to sensibility after the unequal compression, and pain is relieved by a local application of equal parts of turpentine and olive oil with a small quantity of pulverized camphor. The *modus operandi* is not so clear as is the evidence of the immediate relief afforded.

The most valuable use of turpentine is in gunshot and punctured wounds where the tissues around the missile or the instrument are pressed together. The inflammation which takes place around is an effort of nature to supply blood to the part, but this effort is aided by the invigorating influence of a diffusible stimulant such as turpentine.

The practice of sucking punctured or dissecting wounds as soon as an injury is received is very serviceable. While doing so the operator may profitably hold a half teaspoonful of turpentine in the mouth. The senior author has recorded a case of bite of his finger received from a boy with hydrophobia in which the wound was sucked by him while holding turpentine in his mouth.

The immediate application of turpentine and camphor to all contusions or ecchymosed parts relieves the condition generally known as "blood-shot." The best application to bruised cellular tissue such as the eyelids, vulva, etc., is turpentine, but a poultice should supplement this with the heat which supplies nerve power and strength. Hot water to injured tissues has the same effect. At the same time, cold applications are very well borne by the tissues.

The many and various antiseptics applied do not make the same impression as a direct compress and mechanical support, combined with the essential elements of all living tissue, heat and moisture. A

dry dressing is therefore unwise, while all powders are contraindicated.

The following report of an operation for carcinoma of the antrum and of the orbit may serve as an illustration of the value of turpentine. The tissues were mangled and torn in extracting the tumor. The circulation, already greatly impeded by the pressure, had been further obstructed by the preliminary step of the ligation of the external carotid artery. The orbit was so severely dealt with as seriously to endanger the eye. The delicate cellular tissue was so much inflamed as to close the eye, and vision was impaired. The application of the following mixture was used on the day following the operation:

℞ Oil of turpentine,
Olive oil, ... ãã ʒ ij.
Camphor. . . . . ʒ ij.
M. Sig. Apply to the part every two hours, so as to keep it moist.

The oil in this combination must be pure olive oil, and not cotton-seed oil or "sweet oil," as commercial oil is called. The turpentine used is pure oil of turpentine, and not the ordinary "spirit of turpentine" of commerce. In cases of necessity no physician need hesitate to advise a combination of ordinary leaf lard (which may be melted) and turpentine.

The aseptic and curative properties of this combination have been thoroughly tested. The place which it occupies is somewhat different from that of camphorated oil and turpentine as used above, but the osmosis and endosmosis going on in all absorbing surfaces takes up the solution and the blood is restored.

In the prophylaxis of pyæmia and septicæmia, turpentine is indispensable. It is the vegetable substance which more than any mineral or inorganic chemical combination seems to fill all the requirements of strict cleanliness and asepsis; at the same time safety in repeated applications would commend it to the profession as superior to the other antiseptic or sterilizing agents.

According to Dujardin-Beaumetz, terebinthinates introduced into the system, by the skin, lungs, or stomach, enter the general circulation. They then decompose, and while the volatile substances are eliminated by the lungs, the fixed parts are excreted by the urine and exercise their individual properties upon the urinary passages, provided the latter be in a permeable state. In health, and in many morbid conditions, the terebinthinates impart a characteristic odor to the urine, that of violets. In nephritic patients, however, these substances, when administered, gradually fail, with the progress of

disease, to give rise to this odor. Beauvais calls attention to the absence of this odor in the urine in the last stage of Bright's disease. Terebene is the terebinthinate par excellence.

From a study of the various methods of disinfection of the hands, Weir concludes: (1) The solutions of corrosive sublimate are unreliable; (2) disinfection is far better applied, and in the order named, by the use of nascent chlorine, alcohol, or potassium permanganate; (3) chlorine is satisfactorily evolved by the conjoined use of moistened chemical chlorinated lime and crystallized sodium carbonate; (4) of these three procedures, the chlorine treatment is the least hurtful to the hands.

Dunn has drawn the attention of the profession to chinosol as an antiseptic powder. Its properties are classified as follows: (1) Non-caustic, (2) non-toxic, (3) very diffusible, (4) a powerful deodorizer, (5) non-hygroscopic, and (6) it does not coagulate albumin. In regard to the advantage over carbolic acid, it does not injure the skin of the hands; and again, over the bichloride of mercury, (1) it does not harm the instruments, and (2) it does not coagulate albumin. It is a powerful antiseptic, destroying virulent germs in 1:10,000 solutions.

Menge suggests the following way of disinfecting the hands: Thorough mechanical cleansing by means of hot water, alkaline soap, and brush, careful attention being paid to the nails; after that long-continued softening of the hands in water, then thorough disinfection of the skin by means of a watery or weak alcoholic solution of sublimate, soaking in seventy per cent. alcohol, and drying with a sterile towel; finally pouring a paraffin-xylol solution over the hands and then drying with a sterile towel.

The discovery of the presence of the staphylococcus epidermidis albus has given rise to the desire to destroy it completely in preparing the hands of the surgeon for surgical operations. The pathogenic power of this particular microbe has never been proved, but it is known that it is found in the glass drainage tubes in laparotomies, when their contents are carefully examined microscopically. Now this has been construed to mean that the microbe which is ordinarily harmless externally, when allowed to go internally and in constant contact with the denuded surfaces will occasion suppuration by a species of metamorphosis, and often may be observed later as the staphylococcus pyogenes aureus or albus. The most emphatic protests of Lawson Tait and J. F. W. Ross against fear of this microbe has been made known to the world by a comparison of statistics.

In a discussion of the relative merits of corrosive sublimate, simple soap and water, Fürbringer's method, combinations of the two first named with the use of the nail brush and alcohol, and strong solu-

tions of permanganate of potassium, Howard A. Kelly has advocated the latter as the best means of hand disinfection. He has shown that the germs are benumbed by corrosive sublimate, but that a combination with albumin occurs also, and that it is not safe or expedient to employ this substance. After using permanganate of potassium, the stain of which is removed from the hands by oxalic acid, he finds the skin perfectly sterile. The use of permanganate of potassium is safe, and it is bacteriologically exactly what it is clinically, the best disinfectant and deodorant, and at the same time the safest.

No matter what improvements in surgical technique may be made in the future, it is certain that they will always be in the direction of obtaining and preserving more perfect asepsis in the direct handling of the tissues involved in a wound. Not only for the sake of simplicity, but also for the sake of scientific accuracy, is it desirable, in discussing the methods of operating and of preserving asepsis, to discard minutiæ which are unimportant or even irrelevant, and to concentrate our attention upon those details which actually determine the invasion or exclusion of wound infection. That this has been the tendency of surgeons ever since they became thoroughly familiar with the teachings of Lister is shown by the disappearance of the carbolic-acid spray, of caustic and irritating douches, of iodoform powder and medicated dressings as applied to clean wounds, and of a host of applications, each of which has had its advocates as being favorable to all cell growth excepting such as was septic.

Fortunately most of the objects that come in direct contact with wounds made by the surgeon can be rendered perfectly sterile, and not only sterile, but also non-irritating to the tissues. The use of heat, our most reliable disinfectant, has favored the attainment of this object more than any other improvement that has been made, and our instruments, ligatures, towels, and dressings can all be made perfectly sterile.

McBurney has asserted that a dozen men, all of whom have on the same day attended very septic cases, may, without causing the least infection, be present at the performance of any operation if they do not come in actual contact with any person or object directly concerned in the work. There is no difficulty to-day in having absolutely sterile clothing, water, sponges, towels, ligatures, sutures, instruments, and other utensils. If these sterile objects are manipulated with a proper regard for aseptic technique, they never in themselves cause disturbance of healing. The real source of infection of a wound deliberately made by a careful surgeon, who uses perfect materials and handles them perfectly, is to be sought, according to McBurney, either in the skin of the patient or in the hands of those

directly concerned in the operation. Surely, if the skin of the patient were a very guilty party, we should rarely, with such provocation, see perfect healing of a wound. It is also well known that such operations as can be done without having the fingers touch the wound at all give very clean results, and yet the patient's skin is cut and squeezed with instruments and penetrated with sutures at many different points, and the forceps which pick up the skin also pick up the deeper tissues. It is very probable, at least judging by clinical experience, that the patient's skin is seldom an active factor in determining the infection of operation wounds. In fact, the hand is left nearly alone to prove its innocence.

When one considers the number of hands employed in large operations, often as many as ten or twelve, each one of which may be a source of infection; when one considers also the different qualities of the skin, the different characters and habits of the individuals, the different things which they have handled, and even the diseases they may be the subjects of—the problem of providing perfectly sterile hands at every operation becomes appalling.

Many careful observers claim that it is totally impossible to render any hand perfectly sterile. The chief difficulty is that, in all our attempts to sterilize the hands, we are naturally prevented from utilizing our most powerful sterilizing agent—namely, moist heat. Why not, then, cover the hands with a material that can be boiled? This process of reasoning led McBurney, about a year and a half ago, to look carefully into the use of india-rubber gloves. He was aware that they had been used previously for special reasons or on special occasions by others, and he had himself used them and had had one or more assistants use them at different times when the hands had been cracked or fissured or specially infected. But it was only in April, 1897, that he determined to use them systematically. His experience in the matter of wound infection before using gloves had been similar to that of many others. A most satisfactory series of perfect results would be broken in a totally inexplicable manner by a positive wound infection; or a number of wound infections would sometimes follow one another much too closely to be excused as unavoidable accidents.

At the same time he had employed the best-known methods of hand sterilization, and had tested the various materials used at his operations. These were all found to be sterile, but the hands were certainly not uniformly and continuously perfect. In April, 1897, he began the constant use of rubber gloves, and had his first assistant, whose hands especially came in contact with the operation wounds, also use them. At first he thought the difficulty had been solved, for the wound healing was remarkably perfect. Since the middle of

October, 1897, he and all his assistants have worn rubber gloves at every operation of every kind, and the service has been a daily one of great activity. The result has been most gratifying. All the cases operated upon, both in hospital and private practice, from October 19th, 1897, up to the present date, have been carefully observed with a view to the detection of the slightest infection. A large number of the wounds have been immediately closed without other drainage than a small bit of rubber tissue inserted at one or two angles. Solutions of bichloride have not been used in any case, and iodoform has been applied only to wounds already infected before operation and in operations about the rectum. The only douche used has been sterilized salt solution of the strength of six-tenths of one per cent. Excepting that rubber gloves have been worn at every operation, and that the hands have been merely washed in soap and water, no change in any of the methods or details in connection with operations has been made within a year. In a number of cases already infected, such as suppurating and discharging glands of the neck, requiring the use of both knife and curette, the wounds have been completely sutured and closed like originally clean operations.

All of these wounds have healed primarily, and in no one of them has any part of the suture line given way or any discharge occurred. Even actively suppurating spaces, such as occur about a diseased appendix, have seemed, McBurney says, invariably to heal, although, of course, by granulation, in a much more perfect manner than usual. The observations of men in regard to what constitutes wound infection may be different according to the standard of measurement. McBurney, from whom we are still quoting, has made use of the highest clinical standard that he knows of, and he says that he has never before seen such uniformly perfect wound healing of such a high grade. Even primary unions differ in quality. He does not mean to assert that similar perfection has not been reached by others while operating with naked hands, but he personally has never been able before to achieve such results. On this comparatively limited experience he feels justified in saying that, for his own work, no change of methods has ever been so completely and delightfully satisfactory as the use of gloves while operating. The advantages of the method are these: The gloves can be boiled, and so, when the operation begins, they are absolutely sterile. As the gloves are non-absorbent, they must, if they touch no infected object, remain sterile throughout every clean operation. In the course of the operation blood can be rapidly and completely washed off from their smooth surface with a sterile solution. No matter to what previous use the operator's hands may have been put, he may begin his operation without dread that they

may cause infection. The same protection may be secured in the case of assistants and nurses, even when these are inexperienced. Even if he has a suppurating lesion on his own hand, the surgeon may operate with impunity on his patient. Needles can be threaded, instruments can be used, ligatures can be tied just as well and certainly nearly as rapidly with gloves on as without them. One can feel a very feeble pulse perfectly well while wearing a well-fitting rubber glove. The same is true of adhesions, slight differences of consistency, irregularities of surface, etc. One reason for this is that the hands of the operator who wears gloves are never hard and callous or roughened by contact with irritating disinfectants, and the sense of touch is therefore more acute. When a tissue, such as a portion of intestine, is very slippery, a piece of sterile gauze renders it at once manageable. If thick pedicles have to be tied with force, a piece of gauze prevents the ligature from cutting the gloves. If a glove finger is accidentally cut or pricked, the wound is at once closed by putting over it an extra glove finger. The gloves are not expensive, and they last, with daily operating, for from four to six weeks.

If the hands are quite dry, and are then well rubbed with dry sterilized starch, the gloves can be drawn on quite easily even when their interior is moist. Before putting the gloves on, the hands are rapidly washed in an ordinary way with soap and water and then dried. To remove any starch which may have fallen on the outside, the gloved hands are washed off with sterile salt solution. During the operation, blood and other fluids can be very rapidly washed off as often as one chooses, or a fresh pair of gloves can be put on at any moment in case of accidental contamination. During active military and naval service india-rubber gloves would be of the highest value. When rolled up they occupy a very small compass, and can be very rapidly sterilized over and over again in any small vessel which can serve as a boiler.

The best methods of sterilizing the hands would be totally impracticable in a rapidly filling army hospital; but, provided with a few pairs of gloves, the army or navy surgeon need never dread that he may infect the wounds which he treats and makes with his hands.

Treatment.

A proper discrimination between the results of violence and disease forms the basis of treatment for the different stages of wounds. A primary dressing is made with a view to the prevention of trouble beyond that of traumatism; the secondary measures may require a consideration of the changes in the tissues and the consequent gene-

ral derangement of the organism, including both the vascular and absorbent systems. All changes in the organism of a secondary character depend on an impression upon the nerve centres from the local injury, which is propagated by the afferent nerves and the ganglionic nerves to the entire organization, constituting what is styled constitutional disturbance. The action and reaction observed between traumatic lesions and constitutional derangement develop a general effect upon the secretions.

The indications at the outset, when there is local irritation at the point of injury, are to incise the affected part and cauterize with carbolic acid, applying to the circumjacent area an ointment containing equal parts of the following: Ung. hydrargyri, ung. iodi compositum, ung. camphoræ, and ung. belladonnæ.

A poultice of flaxseed meal may cover the inflamed structure, and be renewed frequently, to keep up heat and moisture.

If there should follow much swelling and great tension, incisions should be made freely to relieve the constriction and give an outlet to the serosanguinolent accumulations. This course is more especially indicated when the hand is involved; and when the inflammation extends up the arm, invading the axillary glands, the ointment and poultice should be carried up to the shoulder, so as to cover the entire arm. If the case progresses favorably there may be no accumulation of pus above the elbow, but if abscesses form they should be promptly evacuated and washed out with antiseptic solutions.

It may be laid down as a general rule for our guidance that any original or secondary purulent focus should be freed from septic matter, in whatever form it may exist. If not accessible by curetting or swabbing out, then we may avail ourselves of syringing with those antiseptic solutions which are least likely to do harm by absorption, such as peroxide of hydrogen, permanganate of potassium, and Lugol's compound solution of iodine. In the event that blood clot has remained in the womb after labor or abortion, and is undergoing decomposition, we have a decided preference for a strong solution of chloride of sodium, as it conduces best to dissolving the blood clot. This holds good in the case of sanguineous deposits in the abdominal cavity, in hæmatoma wherever found, and in the accumulation of menstrual fluid, though there may be no coagula to dissolve, and whenever a septic process may result from the collection of blood in the tissues. The solutions of carbolic acid and corrosive sublimate should not be used, as they may prove detrimental by absorption.

The medicinal treatment must be varied, according to the condition of the general system at the different stages of infection, and at the outset calomel and Dover's powder in moderate doses, followed

by Epsom salts, with senna tea, are usually indicated. After free purgation, it is found that quinine and phenacetin have a most salutary effect, and if there is great suffering with pain and restlessness, morphine and atropine may be employed hypodermically to secure rest.

To modify acute inflammation before the suppurative stage, the combination of fluid extract of jaborandi with salicylate of sodium has been attended with most salutary effects, and should be urged to the extent of tolerance. It is to be expected that free diaphoresis and profuse salivation will eliminate to a large extent the poisonous contamination of the vascular system. We had occasion to observe, some years ago, in a case of puerperal septicæmia a most happy and complete transformation from the subcutaneous injection of one-tenth grain of pilocarpine, which produced profuse sweating and relieved the patient of all septic troubles.

After the development of abscesses the chief reliance is upon tonics and depuratives; our experience with the following combination has been quite satisfactory:

℞ Tinct. cinchonæ comp., ... ℥ ij.
Tinct. nucis vomicæ, ... ʒ i.
Potassii chloratis, ... ʒ i.
Aquæ, ... q.s. ad ℥ vi.
M. S. Tablespoonful every three hours.

When the toxæmia progresses in connection with the purulent discharge, it has appeared to be advantageous to introduce into the system gradually an alterative and tonic, such as the following:

℞ Donovan's solution, ... ʒ iv.
Tincture of gentian . . . . . ℥ iiiss.
M. S. Teaspoonful every four hours.

To arrest disintegration of structures, various preparations of iron, such as the albuminate of iron, iodide of iron, and the muriated tincture of iron, with cod-liver oil, lager beer, malt, etc., have been used with benefit in the advanced stages. Everything which can aid the recuperative process is indicated.

The proper sphere of real antiseptic surgery comes into play with pyæmia and septicæmia, as these are preëminently septic developments which require the use of measures to counteract the contamination of the organism. Not only in the local but in the general manifestations is sepsis to be combated, and hence it becomes requisite to correct the secretions and stay the disease of the organs by internal antiseptic remedies. Some have regarded alcoholic treatment as indicated from the outset of the disorder, and that nourishment of a character to prevent the waste of tissues should be combined with

the alcoholic stimulant. The mixture of milk and whiskey or brandy, in form of milk punch, is found to meet the requirements satisfactorily as a routine diet. But it is desirable to supplement this with beef soup, cornmeal gruel, malt, and fresh vegetables, such as Irish potatoes, ochra, and tomatoes, suited to the state of the digestive organs and to the power of assimilation. It is a matter of preëminent importance to sustain the physical organization throughout the continuance of the septic process.

A case came under our observation in the later stages of pyæmia. There had been a bruise of the finger, which swelled. An incision in it was made at the time of great tension on the tissues. The patient had not slept well for three or four days. Calomel and bicarbonate of sodium, of each five grains, were administered three times. Catharsis appeared in the form of four copious discharges from the bowels.

℞ Iodide of potassium, ... ʒ i.
Salicylate of sodium, ... ʒ ij.
Fluid extract of jaborandi, ... ℥ iss.
Simple syrup, ... q.s. ad ʒ iv.
M. S. Take one teaspoonful every three hours in half a cupful of water.

The hand and arm were poulticed with flaxseed to the elbow.

In less than twenty-four hours the patient was much improved and able to sit up. The lymphatic glands decreased in size. We kept him under treatment continuously for twenty-six days. The finger was amputated at the carpometacarpal articulation. After amputation a strong solution of carbolic acid was used. Iodoform moist gauze and cotton and bandage constituted the dressings, which were changed the second day. No stitches were used, because it was thought best to let the wound heal by granulation. There was no perceptible sepsis, but pus from healthy granulations appeared.

Mrs. ——, aged 37, married and pregnant three and a half months, had septic symptoms following a wound from a fish bone in the right thumb. The wounded part was swollen and of a dark purplish color. The patient had a temperature ranging from 99° to 101° F. The pulse was not over 100 at any time. This condition existed about four weeks.

The case was found to be one of pyæmia; pus had burrowed in the thumb and along the line of the muscles. The necrosis of bone required amputation at the carpometacarpal articulation. The recovery was complete and the present condition is good. There was no further pus formation, except once in the breast, which had never given trouble before.

W. D. V——, a vigorous man, aged 30 years, had received a slight abrasion upon the ball of the right thumb from the edge of a tin can about two weeks before, which led to some irritation and swelling, followed by febrile disturbance. We were called to see him four or five days later, and found him suffering with symptoms of lymphangitis of the right forearm, the entire hand being much swollen, and a

reddish streak extending up the palmar aspect of the forearm. A general antiphlogistic and anodyne treatment, with poultices to the hand, was followed by the administration of muriated tincture of iron, quinine, and chlorate of potassium. An incision was subsequently made over the front of the metacarpal articulation of the thumb, and also over the dorsal aspect of the wrist, to relieve the tension of these parts, with a continuation of the poultices to the hand and wrist. Swelling of the entire hand and forearm, intense pain, and a temperature of 103° F., were present when the case was first seen by us. The question of amputation was considered on that occasion, as to its probable effect in arresting the further extension of the inflammation. There being no well-defined limitation of the inflammatory process, we concluded that the septic contamination was not likely to be arrested by amputation above the elbow.

A point upon the dorsal aspect of the forearm giving a sense of fluctuation, a free incision was made, which gave exit to a sanguinolent fluid, without any pus, indicating a collection of blood in a circumscribed area. There was later a similar sanguineous exudation in the cellular tissue on the palmar aspect of the forearm in its upper third, which was discharged by an incision. The ring finger being very much enlarged, and the constriction being marked near its metacarpal attachment, an incision was made along its dorsal aspect, which arrested the disintegrating tendency in its tissues.

There was at the end of a week some purulent discharge from the openings which had originally been made at the junction of the thumb with the hand and on the back of the wrist, and these tracts were injected with a solution of peroxide of hydrogen. The inflammation progressed upwards along the arm above the insertion of the deltoid muscle, and eventually there was a collection of pus near the axillary fold, which was evacuated by a free incision over the upper and anterior portion of the biceps.

The arm having rested upon a fold of cotton batting over the mattress at the side of the patient, and being enormously swollen, there was undue pressure upon the internal condyle of the humerus, so that ulceration occurred at this point. It was a veritable bedsore, and assumed the form of an excavated ulcer, reaching to the periosteum. In the mean time the local pressure was relieved by appropriate dressing and the cavity was filled with iodoform gauze. At a later period it underwent marked improvement from the application of a camphorated basilicon ointment on absorbent cotton.

Hitherto the bowels had been torpid from the necessity of administering morphine to secure rest, and a small dose of calomel followed by salts and senna was given occasionally to procure evacuations. When this failed, enemata of soap water were used with good effect.

In the course of two weeks an abscess formed upon the palmar aspect of the wrist, which was discharged by a free incision longitudinally, nearly in the median line and slightly distant from the site of the radial artery.

About the close of December the condition of the fingers and hand threatened sloughing, so that Peruvian bark and charcoal were incorporated in the flaxseed poultices applied over the entire member, and

the suppurating tracts were injected with a disinfecting solution, while the surface was bathed at each dressing with a bichloride of mercury solution.

Early in January the right leg became involved, manifesting great enlargement and pain about the knee. This was smeared with the compound mercurial ointment and covered with cotton, as had been done at an early stage with the arm. Pus eventually formed throughout the structures on the inner part of the thigh, and was discharged by an incision near the knee. There was another purulent focus below the knee, to which exit was given by an incision at the inner border of the gastrocnemius.

The suppurating tracts were now injected with a wash of a teaspoonful of Lugol's solution in a pint of warm water daily, and each sulcus was irrigated with this until the fluid returned without admixture of pus, using about a quart in cleaning the abscess of the thigh.

The general direction in regard to diet was that it should be of nutritious and easily digested articles, beef-soup made with vegetables, soft-boiled eggs, and milk punch being the main reliance. It should be noted that a free use of whiskey had been ordered throughout the entire course of treatment. The patient was now directed to take lager beer *ad libitum*, and it seemed to have a soothing effect at night. Notwithstanding the use of stimulants and alteratives internally and the most rigid antiseptic treatment locally, the condition of the patient progressed from bad to worse, so that about the middle of January the septic contamination pervaded his entire system. He became delirious and had great vital prostration; his temperature was subnormal.

Early in the month of February the alterative combination was discontinued, and the syrup of the iodide of iron was given in teaspoonful doses four times a day. The latter was continued regularly for about a month without any marked benefit.

Lager beer had been used freely, and the patient took it with decided relish. He added to this subsequently the cod-liver oil. Milk punch with eggs has been used as well as other nutritious food, but neither arrested the emaciation from the constant drain upon his system, and his vital forces gradually declined.

In the mean time an abscess formed above the outer extremity of the right clavicle, which was opened and discharged freely, this being the twelfth incision made in different parts of the upper extremity. On March 1st he was using a teaspoonful of albuminate of iron four times a day.

On March 18th it was found that there was a reaccumulation of pus in the former abscess of the thigh, which had ceased to discharge for some weeks, and the orifice had healed up. The cutaneous covering being found to be thinner below the original opening than at the cicatrized point, the former locality was selected for the incision, which gave exit to at least half a pint of pus. The cavity was washed out with the iodine solution, as had been done previously. A pledget of cotton with camphorated basilicon ointment was applied over the opening. As the preparation of cod-liver oil in use gave some repugnance, he was put upon cod-liver oil with creosote as it was thought

that this would prove more acceptable to the stomach. The albuminate of iron, having disagreed with his stomach for some days, was discontinued. Nutritious food with lager beer was ordered as before.

Tuesday, March 21st: The patient has been examined to-day, and the extreme emaciation, with general prostration of his vital powers, gives little hope of recovery. But there is now little purulent discharge from the abscesses above the clavicle and on the inner part of the thigh, which alone remain open. There is an extensive ulceration or bedsore over the sacrum, and also an ulceration along the leg at the outer aspect of the fibula. These are covered with iodoform and vaseline upon cotton, and the patient is turned upon his left side, so as to relieve pressure upon his back, from time to time daily. The only injunction was to give him all the nourishment he could take, and especially milk and eggs, with a liberal use of lager beer. His pulse now counted 110 per minute, and the temperature was 98° F.

Monday, March 27th: There is no very marked change in the general condition of the patient, yet from the improvement in his appetite there is encouragement for perseverance in the sustaining treatment. There was a new suppurating focus noted just at the pectoral border of the right axilla, involving the glandular structure, which was lanced, and about a teaspoonful of laudable pus was discharged. The two openings, one above the outer third of the right clavicle and the other at the inner and lower portion of the right thigh, have almost ceased to discharge pus, and the bedsores on the loins and on the legs are improving. The cod-liver oil with creosote seems to be of service, and milk-punch, eggs, and other nutritious articles are kept up, along with the lager beer. The Huxham's tincture mixture is to be taken in tablespoonful doses.

April 1st: The patient has not lost strength since last report, and the opening in the right axilla has gradually discharged less, so that very little pus escapes now. There is a fistulous tract from the supraclavicular opening to that on the front of the biceps, through which the dilute Lugol's solution passes when injected into either aperture. The same kind of communication is found from the opening above the knee to that below the knee, yet in neither case does the pus seem to have entered the articulation. The bedsores on the loins and legs are now improving under the application of iodoform covered with camphorated basilicon ointment upon cotton. The prospect is now favorable for recovery, after four months of suffering with grave complications.

April 6th: There has not been any notable change in the condition of the patient, but the fact that he has not lost ground is in itself encouraging. His appetite has improved somewhat by the use of the cod-liver oil and creosote, alternated with the mixture of Huxham's tincture, tincture of nux vomica, and chlorate of potassium. He uses also freely the milk-punch and lager beer. There is but little suppuration from either of the openings, and the small glandular abscess in the axilla has ceased to discharge. This was the only indication of lymphadenitis present throughout the progress of the case, and it disappeared when suppuration took place. The bedsores

are improving, and it seems now only a question of time for the recuperative process to restore the patient's strength and flesh.

April 26th: The patient still clings to life, though extremely prostrated and emaciated. He has discontinued medication, excepting morphine at night to procure rest. He takes gr. $\frac{1}{4}$ of morphine and gr. $\frac{1}{100}$ of atropine at intervals of two hours until three doses are taken, and this enables him to sleep the rest of the night. His wounds on the arm and leg still discharge more or less matter, and are syringed out with an antiseptic wash every day. He uses liberally milk-punch made with rye whiskey, and takes lager beer freely. His nourishment has consisted of beef soup, soft eggs, and other easily digested food, of which he takes sufficient to keep up his flesh, but it does not serve for recuperation of his forces. The bedsores on his loins are relieved by turning him upon the left side for a few hours each day, and seem to be slowly improving. The redeeming feature of this case is the man's pluck and hopefulness amid all the discouragements of his situation.

On May 7th it was found that another abscess had formed at the lower and outer part of the right thigh. This being lanced, there was considerable purulent discharge at the time, and continuing afterward. The cavity was washed out with the dilute compound iodine solution daily. This persistent septic process and the extreme emaciation of the patient led to the gravest prognosis in the case, and it was not thought possible to accomplish anything further by medication or surgical procedures. He continued, however, the use of stimulants and nourishment, with morphine at night, for two weeks, when he sank from sheer exhaustion of the vital forces, being reduced to little more than a skeleton with the cutaneous investment.

This protracted case of lymphangitis, with pyæmia, is reported to illustrate the capacity for resistance to disease. It also serves as a lesson in pathology and to demonstrate the various phases of treatment. The history of the case presents many points of interest in connection with pyæmia, and furnishes a typical picture of the progress of this disease. That a fatal end was deferred so long affords conclusive evidence of the efficacy of treatment in the varying developments of the suppurative process. It is clear that death would have occurred earlier without a recourse to these measures, and the case emphasizes the importance of the prompt use of means to avert the fatal results of blood poisoning.

It is necessary to make use of the sweat glands, of the bowels, of the kidneys, of the lymphatic system, and of the nervous system, to eliminate the products of putrefaction known as ptomaïns. For this purpose we have to select medicines known as diaphoretics, cathartics, diuretics, and tonics, as well as alteratives. The whole animal economy is infected in septicæmia and must be treated as a whole. The rôle of baths, ointments, poultices, and of plasters is more evident in pyæmia than in septicæmia.

One of the classical symptoms of septicæmia is a rash which partakes of the nature of the exanthemata. The most interesting explanation of this is that it is caused by the irritant effects of a poison or ptomaïn from the blood eliminated by the sweat glands. The presence of many toxic agents in ordinary sweat has been argued by Arloing, and the proof of this theory is shown by the prompt recovery which diaphoresis is capable of effecting in some cases.

It has been well said that "autointoxication is just as truly a surgical subject and belongs to this realm as much as it does to internal medicine. The sudden suppression of the sweat is likely to force these 'normal' toxic materials back upon the blood, and the stress of their elimination must then necessarily fall upon other eliminatory organs with such possible or probable results as nephritis, pneumonia, and other excretory inflammations. Shock is a depressant and suppressor of normal function, and courts the generation of toxic substances and their non-elimination."

In dealing with incipient peritonitis, or with any inflammatory disease whatever, it is a wise precaution to give a thorough course of calomel or to give two tablespoonfuls of oil and one teaspoonful of turpentine.

Blood-Washing.—From the well-known principle of osmosis and endosmosis has been derived a very important method of eliminating toxins in cases of toxæmia. The most important application of this principle has been in intravenous saline injections for shock and vital depression accompanying any of the wasting diseases. In the following description of blood-washing we have drawn largely from a paper by Hare, of Philadelphia, read before the Philadelphia County Medical Society, March 24th, 1897.

Michaud details fifteen cases in which this treatment was adopted, all of them cases of septic peritonitis following operation. Of these, five recovered. In one case, the patient being in imminent danger, 1,000 gm. of artificial serum at 39° C. were injected, causing an immediate rise of the temperature of four degrees and a slowing of the pulse. The serum was used during three days, at the end of which time the patient was out of danger and recovered. A similar result was obtained after ablation of the Fallopian tubes, several injections being used, together with irrigation of the peritoneum. The artificial serum of Hayem, or simply sterilized saline water, was used. Various accidents were noted—vomiting, pain in the side, plethora, and disturbance of the cerebral circulation. No later complications were observed. The method is excellent, but other means—drainage, irrigation, reopening of the abdominal incision, and the free local application of ice—are to be used concurrently. Monod has had seven

similar cases, with three recoveries. The effects were beneficial, even in the cases that ultimately terminated fatally.

Bovet and Huchard report an interesting case of pyelonephritis occurring in a married woman who had been a sufferer for a long time from a mild albuminuria. The patient became seriously ill from general toxæmia; fever developed, the urine became scanty and albuminous, the tongue was dry, and a large number of casts were found in the urine. The pulse rose to 130; the respiration to 28. Under these circumstances it was considered wise to inject a considerable quantity of normal salt solution. Between April 20th and October 15th the patient received injections subcutaneously twenty-five times and by the rectum about twenty times. The quantities injected under the skin varied from three ounces to two quarts a day, and the urine increased correspondingly with each large injection.

A second case is reported in which there was uræmia with general anasarca. As a result of this treatment the conclusion is reached that hypodermoclysis is an exceedingly valuable procedure.

Usually as the injection is given the patient at once shows signs of improvement, but in from two to thirty minutes he develops a severe rigor, with a strong, rapid pulse, followed in half an hour by great flushing of the skin and then profuse sweating, with greatly increased urinary secretion. Sometimes quite a marked febrile movement takes place. Several hours afterwards the patient reports himself as greatly improved.

Hare's cases were as follows: A man over sixty years of age developed acute toxæmia, with high fever and coma, owing to the sudden extension up the leg of gangrene of the toes. At first he could be roused only by speaking sharply to him; later he became still more comatose. His muscles became spastic. Twelve hours after the onset of the toxæmia about one quart of warm decinormal saline solution was injected into a vein of the arm in the course of an hour. The man developed a severe rigor, then broke out in a profuse sweat, and the next morning, ten hours afterwards, was perfectly conscious, said he felt first-rate, but later in the day he became comatose again and died. He was doomed from the first because of his gangrene.

The second case was that of a man with chronic parenchymatous nephritis, who came into the hospital with twitching of his muscles and semicomatose. He had passed scarcely any water for several days. He had had constant headache for six months, and was markedly œdematous from head to foot. He was too weak to be bled, or to be purged, or to receive pilocarpine, and seemed too ill for a sweat from a hot pack. One quart of hot saline solution was injected into a vein of his arm. He also had a mild rigor followed by a sweat, and

in three hours thirteen ounces of urine were obtained from his bladder. The next day he said he had no headache, no dizziness, no pain anywhere, and felt no discomfort. His dropsy was not increased. Ten days later, as his uræmic condition seemed to be returning, the injection was repeated, with similar results.

The apparatus which Hare uses is constructed as follows: A glass container, such as is used for irrigation purposes in antiseptic surgery, is set in a frame in order that it may stand on a table rather than be hung against the wall. To the bottom of this container is attached four or five feet of red Para rubber hose, and in the end of this rubber hose is inserted a plain glass cannula; a clip is placed upon the hose in order that the flow may be controlled, and the cannula, with the tube that has been attached to the blood-vessel, is joined to the tube running from the irrigator at the moment when they are both completely filled with liquid, so that no globule of air will be contained in the tube.

W. McKeown considers that theoretically and practically, the principles of osmosis offer the best results, being founded on the fact that toxins are dialyzable; the antitoxins not being so, remain in the circulation undisturbed. The procedure is a simple one: The blood is diluted by the intravenous injections of a decinormal salt solution and the rectum is filled with a saturated solution of magnesium sulphate; thus are furnished the conditions necessary for dialysis, viz., two fluids of different degrees of concentration on either side of an animal membrane (the rectal wall). He treated two cases on this principle; one of purulent peritonitis, the other of puerperal septicæmia. In both a pronounced chill with hyperpyrexia, followed by a sudden drop of the temperature to normal, with marked amelioration of the general condition, was the immediate sequence of each injection. This treatment should be available in all conditions due to the presence of a poison circulating in the blood, which is capable of being dialyzed.

Tuffier has practised intravenous injections, both for hemorrhage and for toxæmia, in fifty cases, including two cases of tetanus (after preliminary bleeding), and found that the first effect was to restore the normal arterial pressure and diminish the frequency of the heart's action; the second, to cause diuresis.

Proben, in a case of eclampsia, injected two quarts of normal saline solution; the urine had been almost totally suppressed, with one hundred per cent. of albumin, but within twenty-four hours the woman passed one hundred and nine ounces.

Berlin has reported the case of a woman who, three days after vaginal hysterectomy, manifested such violent symptoms of sepsis that recovery seemed absolutely impossible. The belly was distended

and painful, and there were very marked subnormal temperature and frequent vomiting. On the fourth day the patient seemed to be about dying, whereupon Berlin gave an intravenous injection of a little over a pint of artificial blood serum, and shortly afterwards repeated this injection, using not quite two pints. Marked cyanosis and increased gravity of the symptoms followed at once, but shortly there was decided improvement and the patient recovered, being completely convalescent by the twelfth day of her illness.

Segond stated that he had used injections of artificial serum for four years in all major operations, and had been able to save many cases of severe hemorrhage by this means. He also stated that in cases of severe sepsis these injections were potent.

Antistreptococcic Serum.—It is now generally believed that erysipelas, puerperal fever, and many septicæmias are due to the action of streptococci of the same or closely related species, and that these germs often attack the weakened tissues and complicate such diseases as scarlatina, diphtheria, tuberculosis, and the like. It was early perceived that a serum efficacious against these germs or their toxins would have a wide field of usefulness. Marmorek first succeeded in producing such a serum, which is now prepared in this country and is being quite extensively employed. While we cannot yet come to a positive decision regarding its merits, the results following its administration in cases of puerperal fever, erysipelas, peritonitis, and other forms of septic poisoning are indeed very encouraging.

A theory based upon the claim that all diseases have their origin in the introduction of germs of one or another order may prove the most satisfactory explanation of the disorders of the physical organization, and should it be made apparent that every special disease has its specific bacillus, science will have made an immense stride in pathology. But when the microscope and other means of investigation shall have demonstrated this as a fact, the more practical and useful discovery of remedies adequate to the destruction or elimination of these bacteria appeals with urgency to the therapeutist; and thus far the bacteriologists have signally failed to point out the curative processes which may meet the requirements. Much is expected from scientific bacteriology, and we are anxiously looking for a solution of the problem of curing disease by germicides, in some way which shall not interfere with the vital functions of organs or tissues involved.

Marmorek's antistreptococcic serum may therefore be tried in suitable cases in doses of from 5 to 40 c.c. Treatment with nuclein is less promising. Hypodermoclysis of decinormal salt solution is

probably effective in eliminating ptomaïns by rapid excretion through the kidneys.

Inflammatory processes, wherever located, are accompanied with pain, from the entrance of the sensory branches of the nerves into the organs; and the means which are adopted for the relief of the inflammation must include the control of the neurotic disturbance by combating this pain. It is a fair inference that all agencies for the mitigation of pain have a curative effect upon the structures involved in disease. The reciprocal influence of body and mind, in the progress of most physical disorders, depends upon their connection through the nervous system. The psychic characteristics of neurotic patients must be taken into account in the management of surgical disorders, just as in medical cases, and much depends upon the mental state of one who has undergone a grave surgical operation. The enervating influence of depression of spirits in the nervous system should be obviated by pleasant surroundings in the after-treatment.

The fountain-head of energy for all the functions lies in the nerve centres; and by controlling emanations from this source of power, the vital forces will be propagated, with regularity and uniformity, to all the remote parts of the physical organization. On the contrary, a harmful influence disseminated from the nerve centres entails disease in the different organs.

The means to be adopted for averting injurious impressions on the nerve centres, and the measures to be used for the correction of their derangement, make up the whole prophylactic agency of hygiene, and include all the therapeutic appliances in the treatment of diseases, as well as the application of surgical measures.

Close observation of the various modifications of the nerve elements on the physical organism should reveal its direct influence in surgical pathology, and lead the surgeon to the adoption of proper means of relief.

Lymphangitis.—In lymphangitis the essential lesion has been shown to be a growth of virulent microorganisms within and along the line of the deep lymphatics. From this the main indication for treatment is held to be some antiseptic that will be absorbed by the lymphatics and carried along these channels to destroy the germs. The form of irrigation known as submersion, in warm water or weak antiseptic solution, has been recommended for this purpose. It is applicable: (1) In cases of continued cellulitis in which repeated incisions have been made, through-and-through drainage established, and elaborate dressings persisted in, yet the tissues remain sodden and infiltrated, joints are destroyed, and the loss of the part is imminent; (2) In severe lacerated injuries, including compound fractures, where septic

infection is present, the tissues are widely involved, and the wound has a porklike appearance; (3) For the purpose of maintaining life in tissues where the circulation is cut off by lacerating injuries of the larger blood-vessels, whether infection is present or not. In submersion the diffusion process is into the water instead of the blood. Water alone is healing. Moisture prevents drying of the secretions, relieves tension, and renders the tissues soft. Heat to a surprising degree retains life in tissues that otherwise would be hopelessly lost. Any antiseptic, such as carbolic acid in very weak solution, would be absorbed into the lymphatics and the tissues would be saturated by an antiseptic agent in such strength as to inhibit the growth of germs at their seat of development. Clinically the change in the patient is a prompt drop in temperature, diminished œdema, the wounds clean up and tissues are saved that had seemed already lost.

Under submersion it has been shown: 1. That blood remains fluid and the vessel walls normal in the distal portion of an injured or obstructed blood-vessel; 2. That the heat of a part is very rapidly diminished when the blood supply is cut off, a condition favoring the rapid death of tissue. The case of a trephine button is cited, also the fact that a Thiersch skin graft may live twenty-four hours if kept in decinormal salt solution, and take well when applied. These and many other things would show that cells may live a long time without blood supply, and the use of submersion is based upon the fact that we artificially maintain conditions of heat favorable to the life of the cell until anastomotic circulation can establish itself.

Irrigation by a constant stream has been stated to be based upon the fact that the great object in septic surgery is to obtain good drainage, and that no permanent dressing, no matter how frequently changed, affords perfect drainage, but leaves secretions in contact with the wound for absorption. The measure consists in conducting a gentle stream of 1:1,000 carbolic or 1:10,000 corrosive sublimate to the bottom of a septic wound and allowing this to bathe the wound constantly. The application of this method to cases of pelvic surgery has some mechanical difficulties, and much stress is laid on the proper placing of the irrigating tube of soft rubber at the bottom of Douglas' cul-de-sac, and often of a second tube by means of a Y attachment into the lateral recesses.

Puerperal Septicæmia.—In the state of the system following the lying-in period, whether in the case of miscarriage or natural delivery at full term, we have serious contamination of the vascular and lymphatic systems from the decomposition of blood clots, retained placenta, or ordinary vaginal secretions.

Roswell Park has given special significance to the fact that toxic

effects result from the retention of material in a containing cavity. The symptoms and course are similar to those of an ordinary case of septicæmia.

Kime, of Atlanta, has devised an ingenious form of rubber drainage tube for cases of puerperal septicæmia, whether due to "septic infection" or to "putrid infection." The object of the tube is to maintain drainage of the cavity of the uterus. This drainage tube is to be taken out once or twice in twenty-four hours for cleaning and disinfecting, while irrigation may be made with weak solutions of carbolic acid, creolin, or boric acid—intrauterine irrigation.

The most diverse opinions are expressed with reference to the use of the curette in the treatment of puerperal septicæmia. Many are confident of the advantage of early curetting, but favor only one resort to it. A consensus of opinion may be said to have been expressed in favor of a dislodgment by some method of putrid material accumulated in the womb. The dull curette, having a hollow handle through which a stream of water flows, may be made a very important means of securing this dislodgment.

An antiseptic wash is also a necessity, and cannot be overestimated when properly used for this purpose. The frequent and thorough swabbing out of the womb with a piece of gauze medicated with iodoform, iodine, and carbolic acid may be instrumental in preventing absorption when a neutralization of putrefaction occurs thereby. Again, creolin in water, common salt in water, or permanganate of potassium in water is preferable to the use of carbolic acid or of corrosive sublimate solution in the womb.

A free discharge of solid material or fluid is necessary in cases of irrigation of the uterus. Hence no partial irrigation is to be attempted. The neck of the womb must be sufficiently dilated in order to allow of an unstinted escape of all contained matter. If the cervix should not be dilated, a dilator may be used. Usually the diseased part communicates by a patulous tract with the vagina, but in no case should irrigation be resorted to unless the finger of the operator may be inserted before doing so.

The speculum, applicator, vulsellum forceps, dilator, and curette are the instruments usually required in the ordinary cases of puerperal septicæmia.

But all cases should be studied with reference to the particular adaptation of the operation. A thin and putrid uterus should not be curetted, and simple drainage is all that may be requisite. But an inflamed, thick, muscular uterus, freshly infected, should be scraped and deprived of germs and of the nidus of germs. Then a simple healing agent may complete a cure by local application.

A case of pyæmia after acute *suppuration of the middle ear* was observed by Ropke. The disease was fully developed during the third week of the otitis media. The pyæmia was attributed to syringing the ear with chamomile tea in the acute stage, and also to poulticing. The local mastoid symptoms were largely negative. There was nearly constant pain in the left temple, accompanied by chills, "fork-lightning" temperature, the permanently rapid pulse, enlargement of the spleen, and dry, cracked, thickly coated tongue. Profuse discharges of pus from the necrosed bone tissue necessitated opening of the mastoid cavity and of the antrum for their complete removal. The temperature was reduced after the operation, while the spleen could not be felt. On the tenth day the patient left her bed, and in one month she was dismissed from the hospital entirely well, and with very good hearing in the previously diseased ear.

Saprœmia, because of the fact that the poison is of less intensity, is treated with more promptness but less energy than pyæmia or septicæmia proper. The treatment consists of nutritious diet, early evacuation of all sloughing and decomposing tissue or necrosed bone, active catharsis, thorough diuresis and diaphoresis, and antiseptic and local treatment. The use of calomel gr. i., and bicarbonate of sodium gr. v., every two hours, until six capsules of these ingredients are taken, may be sufficient. At the same time, turpentine, ℥ ij. with camphor, ʒ i., may be applied locally.

Toxicology.

The occurrence of cases of poisoning by dressings used in the treatment of wounds calls for an enumeration here of the symptoms and causes of such accidental poisoning, together with a brief discussion of treatment.

Carbolic Acid.

The minimum fatal dose has been put at 1 drachm, but much larger quantities have been swallowed with recovery under appropriate treatment. The use of compresses of carbolic acid to the skin has resulted in carbolic acid coma.

Employed in vaginal douche in a strength of 1:33, carbolic acid has been followed by the usual symptoms of poisoning.

A child, after circumcision and a dressing with three-per-cent. solution of carbolic acid, died with all the symptoms of poisoning by carbolic acid.

Pathology.—Depression and paralysis of the medulla oblongata and the spinal cord.

Symptoms.—Coma, loss of sensibility and reflexes, inactive pupils, clonic convulsions, stertorous breathing, pulse beat 30–35 per minute, profuse perspiration. As the patient begins to eliminate the poison of carbolic acid, the consciousness is restored but excitement remains.

Antidotes.—Alcohol, vinegar, oils, turpentine. Alcohol when directly applied in a case of fresh burn from carbolic acid will counteract the effect immediately. Turpentine is more applicable later when the carbolic acid has destroyed the epithelium.

The very best proof of this statement is to be found in the case of a woman in our practice who inhaled a combination of alcohol and carbolic acid which was given by mistake for A. C. E. mixture. Very little effect upon her respiration occurred and not more cauterizing effect on the face than that usually seen from chloroform. The accidental poisoning of our patient would probably have resulted but for the alcohol which was in the combination.

In a similar case of accidental burn during the after-treatment of an operation, an immediate resort to the camphorated liniment described above showed the power of oils and turpentine to counteract the caustic effect of carbolic acid. In cases in which the carbolic acid had been detected and this combination was applied with bicarbonate of sodium and spirit of camphor no blister became apparent, but when no antidote was used blebs formed on the skin.

The internal use of this same liniment was resorted to in a case of accidental poisoning from a teaspoonful of carbolic acid taken by a child: the local effect was supplemented by the use of apomorphine gr. $\frac{1}{20}$ to regurgitate the contents of the stomach over the inflamed area. No effect was apparent upon the delicate mucous membranes of the œsophagus, so prone to become contracted by cicatrization.

In regard to the use of vinegar internally, our own experience does not serve us; but the reports of many writers strongly sustain its claim when administered early in cases in which even large quantities of carbolic acid having been swallowed.

The use of sulphates is also advocated on the basis of neutralizing its chemical effects.

Mercury.

The salt of mercury used in surgical dressings is variously called corrosive sublimate, mercuric chloride, bichloride of mercury, perchloride of mercury, hydrargyri chloridum corrosivum (U. S. P.), hydrargyri perchloridum (B. P.). Its chemical formula is $HgCl_2$, and its atomic weight, 270.54.

All should be or become familiar with the appearance of the crys-

tals of this deadly poison. They are octahedra, but may be flattened, right rhombic prisms, if the crystals arise from the evaporation of a solution, whereas after sublimation by heat they are different. It is seven times more soluble in alcohol than in water. The taste of corrosive sublimate is nauseous, styptic, and metallic, remaining for some time in the mouth.

It is not a stable compound but is easily decomposed in the presence of sunlight and chemicals. Particularly in the presence of organic substances, such as albumin present in the tissues, bichloride of mercury is apt to form the insoluble albuminate of mercury. The most important deductions have been drawn in favor of other antiseptics from this fact alone.

Of 368 cases collected by Witthaus from medical papers during this century, 231 have been reported since 1879, while during the decade of 1870–79 only 22 were reported. "The cause of this sudden and large increase is to be found in the very extensive use of solutions of the bichloride as antiseptics."

Witthaus says: "Of the 231 cases reported since 1879, 143 were caused by irrigation of the vagina or uterus or both with solutions of 1:1000 or of still higher dilution in obstetrical and gynecological cases, and of these 48 were fatal."

"In many of the recent cases," he continues, "death has followed surgical operations in which solutions of corrosive sublimate of 1:1000 or 1:2000 have been used, and in which there have been distinct ante-mortem and post-mortem evidences of mercurial poisoning." "Of 172 cases other than surgical or obstetrical, 70 were accidental, 47 suicidal, 15 by administration by quacks, and 27 homicidal, the remainder having no cause assigned. Of the accidental cases, several followed medicinal administration either of solution or of ointment externally applied, or given hypodermically, by the mouth, or by the rectum in the treatment of syphilis. Or it has been taken by mistake for other white powders (Epsom salts, tartar emetic, potassium bromide, sugar, bismuth subnitrate, santonin, calomel), or the solution has been taken for whiskey, etc. Two poisonings, one fatal, were caused by prolonged contact of the solution with the skin."

The antiseptic tablets of bichloride, although usually colored blue, have been swallowed accidentally.

In the form of vaginal douches in parturient cases the same rapid absorption has been observed as in the case of carbolic acid. The amount used in one case was three and three-quarter grains. Death occurred on the tenth day, and was undoubtedly due to mercuric poisoning. In a case of intrauterine irrigation, reported by

Brann, death occurred on the seventh day, after the absorption of five and one-quarter grains.

On the other hand, very large doses have been recovered from, but such cases were treated promptly by skilful physicians.

Symptoms.—A burning sensation in the gullet is felt soon after the poison has been swallowed. Violent symptoms usually show themselves within five minutes, and consist of incessant vomiting, retching, bloody salivation, and pain in the epigastrium.

In cases of surgical and obstetrical poisoning the pain is referred to the intestines and abdomen before the mouth, pharynx, or mucous membranes are affected. The intense nausea of the internal exhibition of this drug may exist temporarily, but should not be considered as a necessary symptom.

Diminution or total suppression of the urine occurs prominently in fatal cases. When the small quantities of urine passed are examined, albumin, mercury, casts, and blood corpuscles are found. The pulse is rapid, small, irregular. The temperature is subnormal.

The symptoms of poisoning by bichloride of mercury usually last from five to twelve days, but death may occur within a few hours. In the case of children the end comes more rapidly.

The many lesser discomforts which are found in poisoning by surgical dressings may be enumerated as headache, nausea, anorexia, and, in the case of minute doses of corrosive sublimate absorbed in wounds from bichloride gauze, salivation, looseness of the bowels, and cramps, all of which are distinctly indicative of a toxic dose.

Pathology.—The various emunctories and glands and the whole body, in fact, are found to contain the mercury in some form. The quantity in the liver, kidneys, muscles, and spleen is more than that in the bile, thyroid, lungs, brain, or bones, while masses become stopped in portions of the large intestine. Six months or longer may be required for the disappearance of these depots of poison in the few cases that recover.

Prognosis.—Death is apt to be the result of mercuric poisoning sooner or later. In cases of surgical poisoning the prompt removal of the cause may be followed by better results.

Treatment.—White of eggs administered early after the ingestion of bichloride of mercury forms an insoluble compound which may be discharged by the bowels, or immediately by a stomach pump, or by the prompt hypodermic injection of gr. $\frac{1}{10}$ of apomorphine hydrochlorate.

In surgical cases we have pointed out that prophylaxis demands a strict avoidance of "the appearance of evil." But when the symptoms detailed occur, wounds may be opened, treated with white of

eggs locally, and thoroughly washed with pure water in order to effect dilution of the bichloride present in the tissues.

The douches of the birth canal, when the offending cause, should be neutralized by similar douches of white of egg and the hypodermic injection of morphine sulphate gr. $\frac{1}{4}$ and atropine sulphate gr. $\frac{1}{150}$. The dilution of any solution remaining in the uterus must be accomplished by free irrigation with hot water. But above all, immediate catharsis should be accomplished; for this purpose oil and turpentine should be used and on no account should a pill containing calomel or any mercurial preparation be given.

The immediate cleansing of the lower bowel by means of enemata of the white of eggs is also indicated, and many gallons of water may be employed in irrigating the rectum.

Iodoform.

This is a combination of iodine and chloroform, the compound being a yellow powder of bad odor.

Symptoms.—The toxic effects of dusting iodoform upon large wounds are shown in a rise of temperature after each dressing, a woebegone, listless expression, and in some cases, uræmic coma. Iodoform poisoning from surgical dressings has been discussed by P. Cheron, of Paris. The symptoms are (1) *Local:* erythematous rash, with erosion, erysipelas, or simulated phlegmon on the face, eyelids, scrotum, etc. The conjunctiva is rarely affected. The eruption very rarely occurs in children; (2) *General Symptoms:* These often appear without the preceding manifestations on the skin.

The temperature is 102° to 104° F. (39° to 40° C.), accompanied with dislike for food, burning sensation in the epigastrum, vomiting, and nausea. Elderly persons and those suffering from renal insufficiency show very violent and even fatal symptoms. Coryza, redness of the conjunctiva, frontal headache, and a metallic taste in the mouth have been observed.

These symptoms quickly disappear after the iodoform dressings are discontinued. Various substitutes for iodoform, such as boric acid, nosophen, aristol, and others have been proposed, but the entire avoidance of powders of any kind in the early treatment of healthy wounds is advisable.

Idiosyncrasy.—There are numbers of people who are unable to bear even a moderate quantity of iodoform. Recently a young man with a very small absorbing surface at the meatus turned deathly sick from the use of a piece of ten-per-cent. iodoform gauze inserted to keep the lips of the meatus apart. He suffered no untoward effects

from the substitution of a similar strip of sublimated gauze. He had always had a great antipathy to iodoform.

It has been recorded in many bedside observations that iodoform is not borne by large freshly cut surfaces in the breast, and the caution above given as to the use of any powder upon fresh wounds is especially applicable after amputation of the mammary glands. The case of an old negro woman operated upon in Atlanta by a competent surgeon in this way for carcinoma has served to emphasize this fact of a susceptibility to iodoform. The wound was large and the flaps were not sufficient to be brought in contact, so that the result was that a large area was expected to be filled by granulations, and iodoform was dusted on this area at the time of the operation and immediately afterwards. The wound was subsequently dressed frequently and each time iodoform and iodoform gauze were used. The usual symptoms of iodoform poisoning supervened and the patient died.

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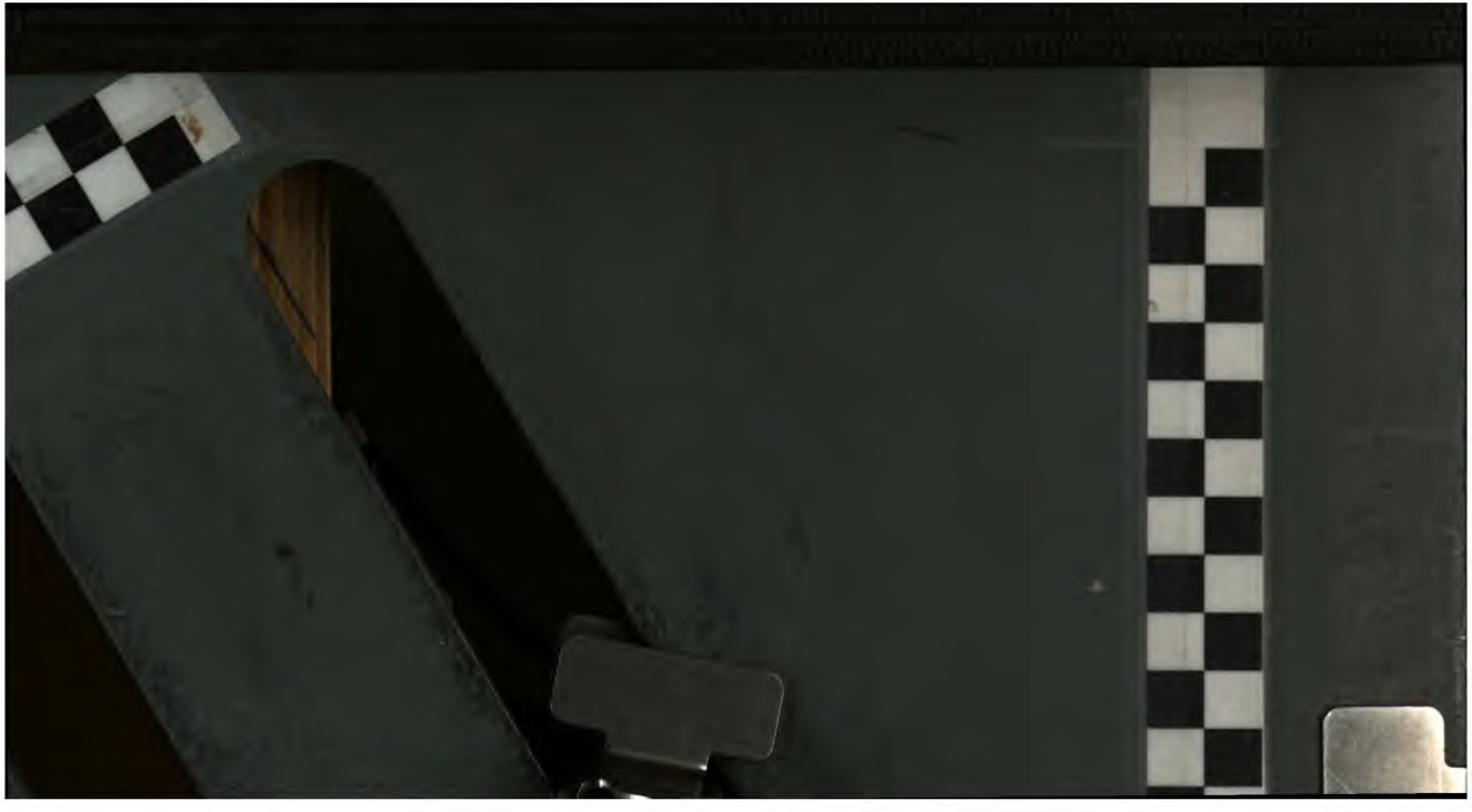
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